STUDIES IN SESQUITERPENOIDS

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C O N T E N T S

PART ONE

SYNTHETIC STUDY OF METHYLCADALENES

PART TWO

CHEMICAL EXAMINATION OF THE WOOD FROM CEDRELA TOONA

Part One

SYSTEMATIC STUDY OF METHYLCADALENES

C O N T E N T S

CHAPTER I

INTRODUCTION

CADALENIC SESQUITERPENOIDS

CADALENE [illegible] ITERP[illegible].

A survey of the literature reveals that truly remarkable progress has been made in the field of sesquiterpenoid chemistry during the past few years. If, on one hand, numerous new types of eco[illegible]u-cidated, on the other hand [illegible] sesqui-terpenoids have been [illegible] knowledge of this inte[illegible].

Until recently, the analysis and elucidation of structure of sesquiterpenoids was hampered by special difficulties. The isolation of individual compounds which usually occur in mixtures of closely related compounds was considerably difficult. Further, with the classical methods alone it was rather difficult to establish the structure and stereochemistry of a compound because of the number of isomeric possibilities. However a fundamental advance in sesquiterpenoid chemistry was brought about by the introduction of highly effective separation techniques such as precise fractionation, adsorption chromatography, gas l[illegible] chromatography (GLC) and thin layer chromatography (TLC). More particularly [illegible] techniques in their preparative scale are regarded as the valuable tools of separation and accordingly they have opened up new possibilities for studying the sesquiterpenes. The use of physical methods[1] such as ultraviolet, infrared,

nuclear magnetic resonance spectroscopy, optical rotatory dispersion and more recently mass spectrometry has greatly advanced and perhaps even revolutionised the successful elucidation of the structure of organic compounds. Actually these physical methods have made the structure determination of a new compound more systematic by offering supporting evidences. By employing most of the above techniques and tools, it has been possible to isolate a number of sesquiterpenes in a pure form and to elucidate their structure in all detail.

Significant progress has also been made in the syntheses of sesquiterpenoids[2]. To quote a few recent examples, we have the syntheses of (±) cadinene dihydrochloride[3], longifolene[4], clovene[5], α-santalene[6,7], cedrol[8], widdrol[9], thujopsene[10], patchouli-alcohol[11], d,l-caryophyllene[12], α-caryophyllene alcohol[13] and longicyclene[14]. As it is not possible to discuss the details of such a wide topic in this Chapter we restrict ourselves to a survey of "Sesquiterpenes of the cadalenic group".

Compounds belonging to this group* possess the

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*The structures given in this Chapter represent the absolute configurations if known.

perhydro-cadalene skeleton and yield cadalene on dehydrogenation. They may conveniently be classified into two types:

1 Cadinenic sesquiterpenoids.

2 Other cadalenic sesquiterpenoids.

CADINENIC SESQUITERPENOIDS

Bicyclic sesquiterpenoids which can be characterised by the formation of the common derivative 'Cadinene-dihydrochloride' belong to this class of compounds which includes the naturally occurring cadinenes and cadinols. If some of the cadinenes and cadinols yield (-)-cadinene dihydrochloride, some others afford (+)-cadinene dihydrochloride or even (±)-cadinene dihydrochloride. The synthesis of (±)-cadinene dihydrochloride has been achieved recently[3]. Ruzicka and Stoll[15] introduced a simple nomenclature making use of the Greek letters as prefixes for distinguishing the various isomeric cadinenes. Motl et al.[16] have introduced a rational nomenclature which is applicable to all cadalenic sesquiterpenes.

CADINENES:

Out of the nine theoretically possible structural isomers of cadinenes, seven are known today. The recent clarifications about the actual structure of 'ε-cadinene' by Westfelt[17] and the purity of γ-cadinene by Sutherland and coworkers[18] demonstrate the difficulties involved in the

separation and characterisation of cadinene isomers. Table 1 describes the physical properties of known cadinenes.

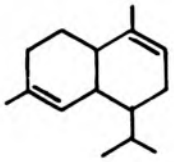
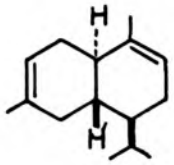
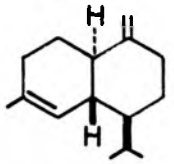
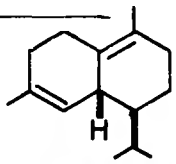
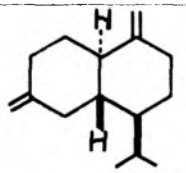
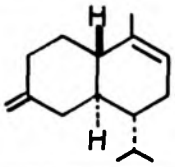
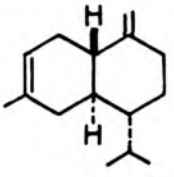
1 α-Cadinene (adina-4, 9-diene)

To a cadinenic hydrocarbon isolated from Eucryphia colensoi Briasco and McMurray[19] assigned the structure I, although the assignment lacks direct chemical evidence.

2 β-Cadinene (Cadina-3, 9-diene)

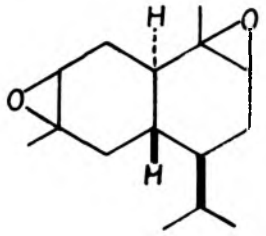
After establishing the carbon skeleton of a cadinene molecule by its dehydrogenation to yield cadalene, identified by its synthesis by Ruzicka et al.[20] what remained to be settled was the position of the double bonds in cadinene molecule. It was in this connection that Campbell and Soffer[21] obtained this hydrocarbon as a principal component (?) by the dehydrohalogenation of cadinene dihydrochloride, and by employing the elegant method of Ruzicka and Sternbach[22] for labelling the nuclear double bonds with additional methyl groups, established the structure of this β-cadinene as II. Later on, the Czech workers[23] reported to have obtained a 'very pure sample' of β-cadinene by fractionation through efficient column. Its presence has also been shown by Herout et al.[24] in the essential oil of Solidago canadensis.

TABLE 1: SURVEY OF THE KNOWN CADINENES

No.	Name	Structure	d_4/t	n_D/t	$[\alpha]_D/t$	Sign of the $[\alpha]_D$ of the dihydrochloride.	Ref.
I	α-Cadinene		0.9190 (20°)	1.5089 (20°)	+70° (18°)	(-)	19
II	β-Cadinene					(-)	18
III	γ-Cadinene		0.9125 (20°)	1.5075 (20°)	+148° (20°)	(-)	23
			0.9189 (24°)	1.5083 (23°)	-153° * (24°)	(+)	28
			0.9252 (20°)	1.5090 (20°)	+2.1 (20°)	±	29
IV	δ-Cadinene		0.9175 (20°)	1.5086 (20°)	+94° (20°)	(-)	23
					(±)	(±)	38
V	ε-Cadinene*			1.5032 (22°)	-15.9 (22°)	(-)	17
VI	γ_1-Cadinene		0.9260 (30°)	1.5155 (26.5°)	-18.9°	+	43
VII	γ_2-Cadinene		0.9168 (30°)	1.5051 (28°)	-40°	+	44

*These sesquiterpenes are not reported to be naturally occurring but have been obtained by other methods.

Sutherland and coworkers[18] have recently shown that the so-called very pure sample of γ-cadinene reported by the Czech workers was inhomogeneous*. Further by isolating a di-epoxide (IIa) obtainable from γ-cadinene, they have characterised this hydrocarbon, γ-cadinene without actually isolating it.



IIa

3 <u>γ-Cadinene (Cadina-4, 10(15)-diene)</u>

The isolation of this hydrocarbon was first reported by Kafuka et al.[25] who established the presence of an exocyclic double bond in it. Later on by employing the technique of fractional distillation and elaborate chromatography Herout et al.[26] isolated this hydrocarbon from <u>Citronella oil</u> in a comparatively pure state. Further, the Czech workers[27] confirmed the presence of the end methylene group by quantitative ozonisation and infrared characteristics (738, 836 and 890 cm^{-1}). The position of the other double bond was fixed as in III by its

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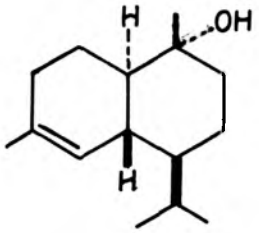
*Taking into consideration the difficulties involved in the separation of these isomers, these authors have doubted the homogeneity of all other cadinenes except δ-cadinene and ε-cadinene.

correlation with γ-cadinol (IIIa), the p-nitrobenzoate derivative of which on pyrolysis yielded this hydrocarbon.



III a

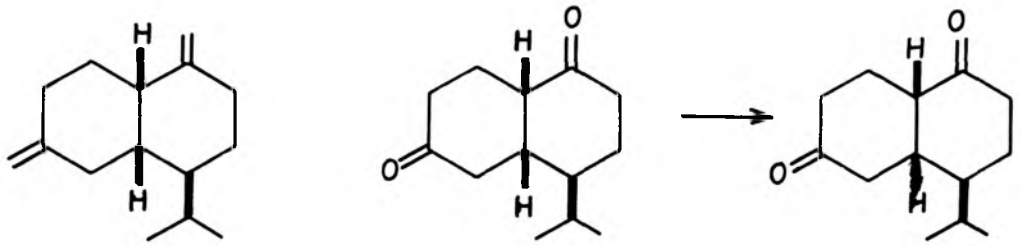
Both the optical isomers of γ-cadinene affording (-)[26] and (+)[28] cadinene dihydrochlorides as well as the racemic γ-cadinene, affording (±)-cadinene dihydrochloride[29] have been reported in the literature.

4 δ-Cadinene (Cadina-4.10(1)-diene)

δ-Cadinene has been found to occur in a number of essential oils e.g. Ylang-Ylang[30], Citronella[26], Sweet flag[31] (Acorus calamus L), Pinus sibirica[32], Juniperous species[33] and Cedrela toona[34] and thus is widely distributed in nature. The Czech workers[35] made an attempt to label the double bonds with additional methyl groups by the usual method but the epoxides were found to be unreactive. Based on this observation and infrared data[36], the above authors advanced structure IV for δ-cadinene. (±)-δ-cadinene (Hysoxylonene) has been isolated by Penfold[37] from rose wood and its identity established by Hildebrand and his co-workers[38].

5 c-Cadinene (Cadina-4(14)-10(15)-diene)

This hydrocarbon so far reported in the literature[28,30] under the name "c-cadinene" has been recently shown[17] to be nothing but (+)-t-muurolene VA in which the two rings are cis-locked in contrast to the cadinene isomers. Thus, c-cadinene has yet to be isolated as a naturally occurring compound. However, this hydrocarbon V has been obtained by the dehydrohalogenation of (-)-cadinene dihydrochloride and its degradation product VC, has been correlated with the degradation product (VB) of (+)-t-muurolene. The synthesis of (+)-[40] and (±)-[3] diketones has been achieved.



VA VB VC

6 γ_1-Cadinene (Cadina-4(14), 9-diene)

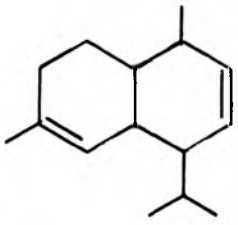
The occurrence of this hydrocarbon in the oleoresin of Hardwickia pinnata was reported by Ayub Dev and Guha[41]. Later on, it was isolated by Bhattacharyya et al.[42] who on the basis of ozonolysis and infrared data established the presence of an end methylene group. The position of the remaining double bond was located[43] by the labelling method, thus enabling its formulation as VI .

7 γ_2-Cadinene (Cadina-3, 10(15)-diene)

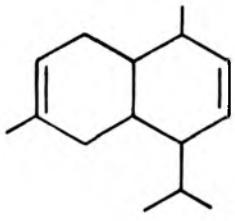
From the Indian vetiver oil another hydrocarbon belonging to the antipodal group (i.e. affording (+)-cadinene dihydrochloride) was isolated by Bhattacharyya et al.[44]. Ozonolysis and infrared data disclosed the presence of a vinylidene group while the usual labelling method enabled them to fix the position of the other double bond as in VII.

Sumbulene:

The isolation of a hydrocarbon sumbulene was reported by Dyson[45] from the essential oil of Ferula sumbul Kock. Sumbulene, d_4^{20} 0.8993, n_D^{20} 1.4962, $[\alpha]_D^{15}$ +10.21 afforded (?) cadinene dihydrochloride. Two alternative structures (VIII) and (IX) have been proposed for sumbulene.



VIII



IX

CADINOLS

Of the twelve theoretically possible structural isomers of cadinol, only three have been found in nature

and so far the constitutions of two have been elucidated. Cadinols affording both (-)-and (+)-cadinene dihydrochlorides are reported in the literature[23,32]. Table 2 summarises the physical constants of the known cadinols.

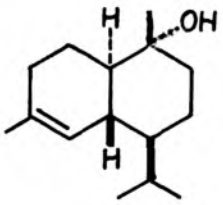
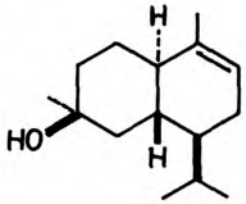
[1] α-Cadinol

Plattner and Narcus[46] were the first to isolate α-cadinol from Javanese citronella oil. Later on, it has been shown to be present in the essential oils of Chamaecyparis species[47,48], Leocallitropis araucariodes[49] and Juniper berries[16]. The Czech workers[16] fixed the position of the only double bond as in I by employing the labelling method. The tertiary hydroxyl group present in α-cadinol was shown to be equatorial by its ease of esterification. Joffer et al.[50] also arrived at the same structure independently by following the labelling method.

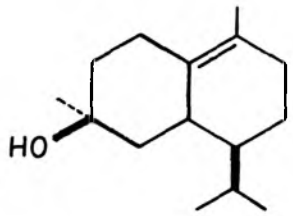
[2] δ-Cadinol

Isolated under different names from Pilgerodendron uviferum[51], Juniper species[16,52], Pinus species[32,53], Cedrela odorata[54] and falsecubebs[55], but finally identified as δ-cadinol which appears to be widely distributed in nature. The structure IIa assigned to δ-cadinol by the Czech workers[16] was shown to be erroneous by Dauben et al.[56] who, on the basis of NMR data coupled with hydroboration

TABLE 2: SURVEY OF THE KNOWN CADINOLS

No.	Name	Structure	m.p.	$[\alpha]_{D/t}$	Sign of the $[\alpha]_D$ of the dihydrochloride.	Ref
I	α-Cadinol		72.5°	-39.4°	(-)	46
			74.5°	-47°		23
II	δ-Cadinol		139-40°	-109°	(-)	23
			141°	+118.4°	(+)	51
III	A new Cadinol	?	78.5 - 79°	-89°		23

and optical rotatory dispersion studies put forward the structure II for δ-cadinol. Sesquigoyol[53] (≡ Torreyol)[57] has been shown to be nothing but (+)-δ-cadinol.



IIa

[3] A crystalline cadinol[48,58,23], m.p. 78.5 - 79°, $[\alpha]_D$ -89° isolated by two groups of workers, from Chamaecyparis pisifera[48] has not been studied in detail.

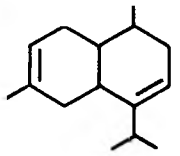
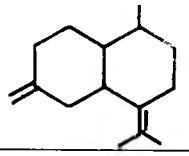
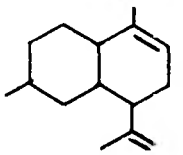
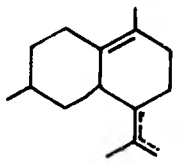
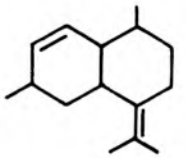
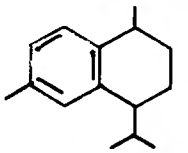
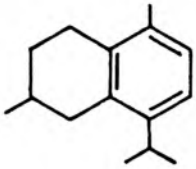
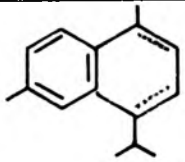
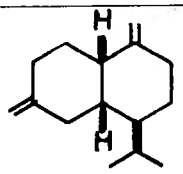
[4] Taiwanol

A liquid sesquiterpene alcohol, taiwanol d_4^{30} 0.9692, n_D^{30} 1.5045, $[\alpha]_D^{30}$ -42.56° obtained[59] from Taiwania Cryptomerioides hayata was characterised as its phenylurethane m.p. 134.5° and yielded cadinene on dehydration.

OTHER CADINENIC SESQUITERPENOIDS

These bicyclic sesquiterpenes have the double bonds situated at positions different from those of cadinenes and hence the characteristic cadinene dihydrochlorides are not formed. The physical constants of the known compounds are described in Table 3.

TABLE 3: SURVEY OF THE MORE CADINANIC HYDROCARBONS OTHER THAN CADINENES

No.	Name	Structure	d_{4}^{t}	n_{D}^{t}	$[\alpha]_{D}^{t}$	Ref.
I	Isoziagiberene*		0.9052 (20°)	1.5021 (20°)	-38° (22°)	61
II	Sesquibenihene		0.9560 (29°)	1.5033 (29°)	-4.1° (29°)	62
III	A new hydrocarbon.		0.9220 (30°)	1.5029 (31°)	+68.24° (25°)	63
IV	Metrosiderine		0.9155 (20°)	1.5041 (20°)	-8.05° (20°)	64
V	Rupatene		0.9026 (27°)	1.5012 (26.5°)	+16.25°	65
VI	Calamenene		0.9265 (20°)	1.5188 (20°)	-50.6° (20°)	56
VII	Isomer of * Calamenene		0.9328 (20°)	1.5240 (20°)	-	60
VIII	Calacorene		0.9399 (20°)	1.5271 (20°)	+52.1° (22°)	31
IX	d-Amurolene		-	1.5049 (22°)	+50.7° (22°)	17

*Not naturally occurring but obtained by other methods.

HYDROCARBONS*

[1] Isozingiberene

A new sesquiterpene hydrocarbon has been found to co-occur with zingiberene in ginger oil. This new hydrocarbon termed isozingiberene afforded a crystalline dihydrochloride m.p. 172°. Soffer and coworkers[61] examined its constitution and assigned the structure I based on the evidence furnished by the labelling method.

[2] Sesquibenihene

Katsura[62] reported the isolation of a sesquiterpene hydrocarbon sesquibenihene from the oil of Chamaecyparis formosensis and the structure II has been assigned to it.

[3] A new cadalenic sesquiterpene

A new cadalenic hydrocarbon was reported by Bhattacharyya et al.[63] from the South Indian vetiver oil. Ozonolysis data coupled with the labelling method enabled them to advance structure III for it.

[4] Metrosiderine

Corbet and Manger[64] obtained this hydrocarbon from Metrosideros umbellata. The results of their ozonolysis experiments led them to assign the structure IV to it.

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*Recently T. Nasamune et al.[60] have reported the isolation of cadalene from the steam volatile oil obtainable from the methanol extract of Dictyopteris divricata. We have also isolated cadalene from the pet. ether extract of Cedrela toona. (Pl. see Ch.II of Part II).

[5] Eupatene

The isolation of this hydrocarbon eupatene was reported by Bhattacharyya et al.[65] from the oil of Eupatoriumodoratum. Structure V has been suggested for this hydrocarbon based on the ozonolytic experiments.

[6] Calamenene

The presence of this hydrocarbon has been demonstrated in a number of essential oils e.g. Juniperous species[33a,66], Sweet flag oil[31] (Acorus calamus L.), false cubebs[55], Baccharis genistelloids[67] and Cedrela toona[34]. The structure (VII) originally proposed by Triebs[68] was shown to be erroneous by the czech workers[31] who established the alternate structure VI and later, it was confirmed by its synthesis[69]. It was in this connection that the isomer of calamenene (VII) was synthesised by them.

[7] Calacorene

The cadalenic hydrocarbon calacorene was isolated by Czech workers from the Sweet flag oil[31] (Acorus calamus L.). The structure VIII was advanced for it based mainly on its ultraviolet spectral data and its conversion to calamenene by hydrogenation.

[8] ε-Muurolene

From the essential oil of Pinus sylvestris, a sesquiterpene hydrocarbon termed ε-muurolene has been

isolated by Westfelt[17]. (+)α-muurolene afforded a mixture of (+)-muurolene dihydrochloride and (-)-cadinene dihydrochloride in the ratio of 2:1 on treatment with hydrogen chloride in ether. Based on the evidence furnished by the ozonolysis experiments and other chemical data, structure I has been assigned for it where in the two rings are cis-locked in contrast to normal cadinenes.

Alcohols

Table 4 describes the physical constants of the known alcohols.

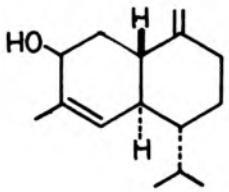
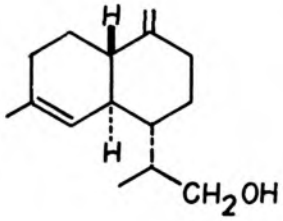
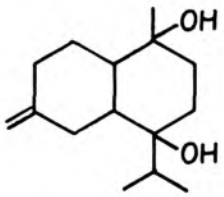
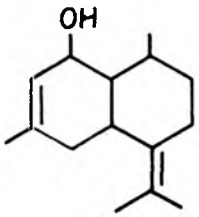
1 Khusinol

From the vetiver oil of the North Indian variety Bhattacharyya and co-workers[28] isolated another sesquiterpene alcohol khusinol. Oxidation of its dihydroderivative afforded an α,β-unsaturated ketone revealing the nature of the hydroxyl group as secondary. The usual labelling method fixed the position of the hydroxy group. Further, its conversion to (-)-γ-cadinene Ia, coupled with the above data permitted the above workers to assign the structure I to it.

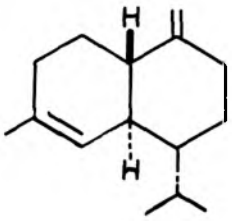
2 Khusol

Bhattacharyya et al.[70] isolated a sesquiterpene alcohol khusol from the vetiver oil of South Indian origin. Ozonolysis experiments revealed the presence of an end methylene group. The nature of the hydroxyl group was proved

TABLE 4: SURVEY OF THE KNOWN CADALENIC ALCOHOLS OTHER THAN CADINOLS

No.	Name	Structure	m.p./ b.p.	$[\alpha]_{D/t}$	Ref.
I	Chusinol		87°	174.4°/ 25°	28
II	Chusol		101-102°	-137°/ 27°	70
III	Calamendiol		169°	-4.4°	68
IV	Articulol		130-32°/ 1 mm.	-22°	71

to be primary by the conversion of its tetrahydro derivative into an aldehyde. Further, Khusol was converted through its p-toluene sulphonate to (-)-γ-cadinene (Ia) of known absolute stereostructure. The above evidence, supported by the NMR data, enabled the above workers to assign structure II to it.



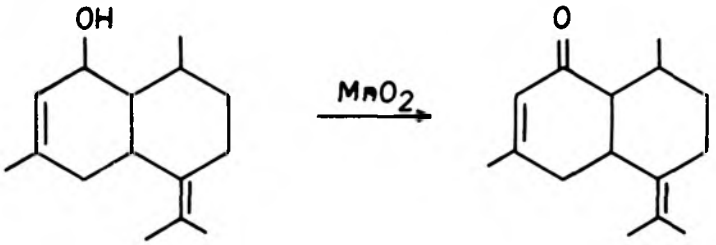
Ia

3 Calamendiol

The essential oil of Acorus calamus L. contained an alcohol, $C_{15}H_{26}O_2$, termed as calamendiol. Triebs[68] examined its constitution and assigned a tentative structure III.

Articulol

Plader and his co-workers[71] have reported the isolation of a sesquiterpene alcohol, articulol from the essential oil of Cyperus articulatus L. Manganese-dioxide oxidation of articulol furnished articulone (V), an α-β-unsaturated ketone which co-occurs with this alcohol. Based on this data structure IV has been put forward for this alcohol.



IV V

B.P. 104 - 106° / 0·1 mm.

$[\alpha]_D^{20}$ - 26·6°

OTHERS

Besides the hydrocarbons and the alcohols, only one ketone has been reported so far.

Articulone

From the essential oil of *Cyperus articulatus* a sesquiterpene ketone named articulone has been isolated by Pinder *et al.*[71]. Ozonolysis experiments supported by the spectroscopic data have enabled the above authors to advance structure V for it.

STEREOCHEMISTRY AND ABSOLUTE CONFIGURATION OF CADINENIC SESQUITERPENES

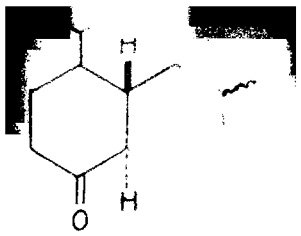
By a study of the physical properties of tetrahydrocadinene and tetrahydroselinene, Ruzicka et al.[72] proposed a cis-decalin structure to cadinene. It remained accepted till 1954 when Rinaker et al.[73] showed that cubebol possessed a trans-decalin system proving the previous method to be unreliable.

An important contribution to the determination of the stereochemistry and absolute configuration of cadinenic

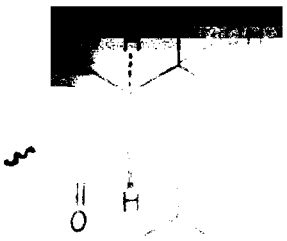
sesquiterpenes came from the Czech workers[74]. Since most of the cadinenic sesquiterpenes afforded (-)-cadinene dihydrochloride or dihydrobromide, the application of the physical methods such as X-ray diffraction and optical rotatory dispersion appeared more useful. Accordingly, X-ray diffraction studies on (-)-cadinene dihydrobromide by Hanic[75] revealed that both the rings in cadinene dihydrobromide are trans-fused, all the three alkyl groups equatorial and the two halogens axial being placed on the same side of the molecule. In full support of the assigned stereochemistry the dipole moment measurement results[23] (cadinene dihydrochloride 4.060, cadinene dihydrobromide 4.200) were in good agreement. Thus, the above facts enabled to generalise that all cadinenic sesquiterpenes that afford (-)-cadinene dihydrochloride or dihydrobromide, must possess the same configuration at C_1, C_6 and C_7 since these carbon atoms are not involved in the formation of the derivative. Of these three asymmetric centres, determination of absolute configuration at any one centre would suffice to determine the absolute configuration at the other two centres. This was achieved by two methods.

(i) Optical rotatory dispersion method

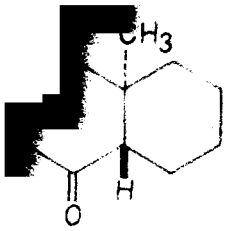
The Optical rotatory dispersion curves of the two ketones (I) and (II) obtained during the investigation[16] on



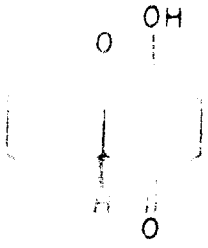
I



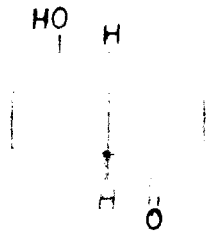
II



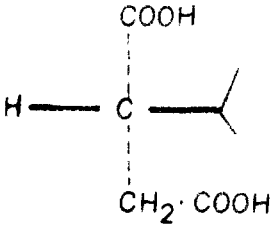
III



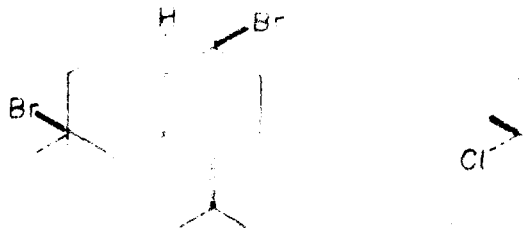
IV



V



VI



VII VIII

α-cadinol were compared by Djerassi et al.[16] with a reference compound[76] (III) of known absolute configuration. Further, from this comparative study it was shown that the rotatory dispersion curve of (II) was of the same type as the reference compound while that of (I) had the opposite sign.

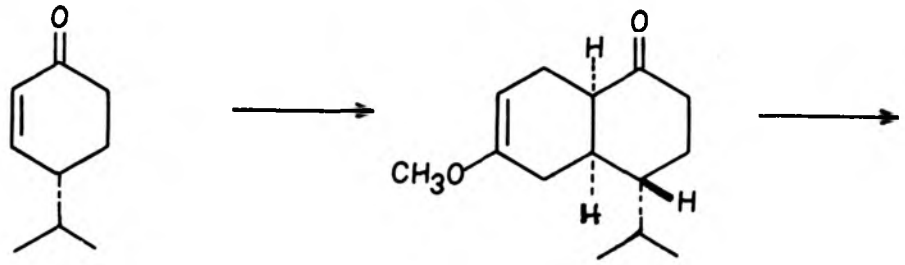
The Optical rotatory dispersion measurements of two hydroxy decalones (IV) and (V), whose absolute configuration was determined by Prelog[77], served as confirmatory evidences for the above conclusions.

(ii) Chemical method

The absolute configuration at C_7 could be settled by obtaining an optically active isopropyl succinic acid from any cadinene, since all the cadinenic sesquiterpenes possess the isopropyl group at that asymmetric centre. Thus by the oxidative degradation of β-cadinene Sorm et al. obtained "isopropyl succinic acid" which was found to be identical with D(+)-isopropyl succinic acid (VII) prepared by Fredga et al.[78]. Hence the isopropyl group in all compounds affording (-)-cadinene dihydrohalide (VII) must be -oriented as in VII .

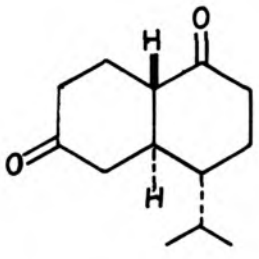
Since a number of cadinenic sesquiterpenes affording (+)-cadinene dihydrochloride (i.e. equal and opposite sign) have been reported recently, it follows from the above findings that these must be represented by the antipodal configurations.

Soffer and his co-workers[40] recently established a synthetic correlation between the cadinenic sesquiterpenes and monoterpenes of the p-menthane series. Thus (-)-cryptone of known absolute configuration X, in the Diels-Alders reaction with 2-ethoxy butadiene 1-3, gave the enol ether XI which on acid hydrolysis and epimerisation in alkali afforded XII as the main product. This diketone was found to be the optical antipode of the degradation product (XIII) of '(-) δ-cadinene'.

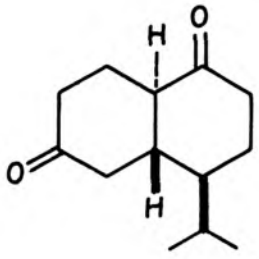


X

XI



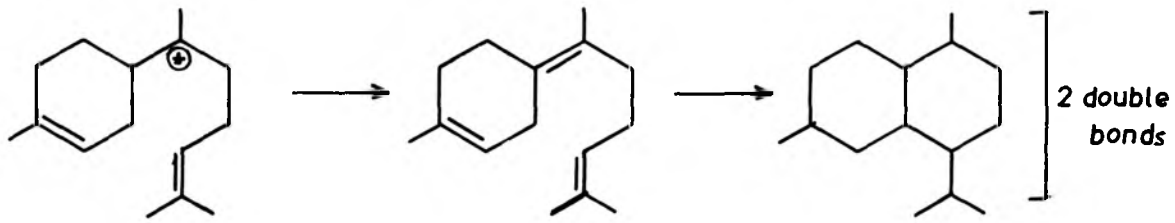
XII



XIII

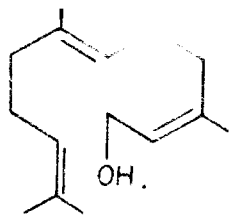
Biogenesis

Since the postulation of the biogenetic isoprene rule by Ruzicka[79] in 1953, considerable progress has been made in the study of the biogenesis of terpenoids. It now appears certain that immediate precursor in the biogenesis of isoprenoids is mevalonic acid[80]. Hendrickson[81], in 1959, further elaborated the ideas of Ruzicka by considering the stereoelectronic factors in the cyclisation of both cis-and trans-farnesols. In the present discussion we would like to restrict ourselves on the possible biogenesis of cadinenic sesquiterpenes. Ruzicka had considered that cadalenic sesquiterpenes arise from farnesol by a 1,6-cyclisation to the ion I which would lead to bisabolene (II) and related compounds and these could further cyclise to cadalenic sesquiterpenes.

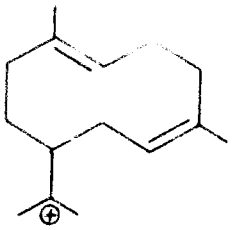


I II III

However, it appears more attractive to postulate that the scheme shown in the Chart 2 may actually be the pathway followed by various cadinenic sesquiterpenes. The

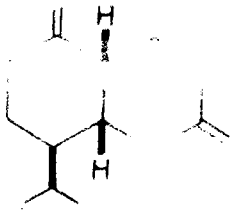


Cis - FARNESOL IV



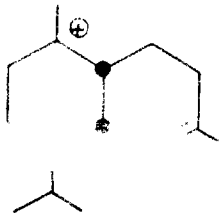
V

VI

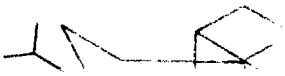


muurolen

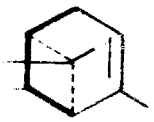
VIII



VII



IX



X
Copaene

XI XII

INENIC AND
CADALENIC SESQUITERPENE

ENES

SESQUITERPENES

formation of species VII was first postulated by P. de Mayo[82] in his study of the biogenesis of helminthosporal. As can be seen the carbonium ion in VII can lead to copaene* (X), muurolenes (VIII) and cadinenes.

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*Please see, Chapter III of Part II for the structure elucidation of copaene.

REFERENCES

1 K. Biemann in Elucidation of Structures by Physical and Chemical Methods (Edited by K.W. Bentley) part one, p.260. Technique of Organic Chemistry (Edited by A. Weissberger) Interscience, New York (1963).

2 J.M. Mellor and S. Munavalli, Quart. Rev. 18, 270 (1964).

3 M.V.R.K.Rao, G.S.K.Rao and Salih Dev, Tetrahedron Letters 27, 27 (1960).

4 E.J. Corey, M.Ohno, R.B. Mitra and P.A. Vatakencherry, J. Am. Chem. Soc., 86, 478 (1964).

5 P. Doyle, I.R. Maclean, W. Parker and R.A.Raphael, Proc. Chem. Soc., 239 (1963).

6 E.J. Corey, R. Hartmann and P.A. Vatakencherry, J. Am. Chem. Soc., 84, 2611 (1962).

7 G. Brieger, Tetrahedron Letters 28, 1949 (1963).

8 G. Stork and F.H. Clarke Jr., J. Am. Chem. Soc., 83, 3114 (1961).

9 C. Enzell, Tetrahedron letters 5, 185 (1962).

10 W.G. Dauben and A.C.Ashcraft, J. Am. Chem. Soc., 85, 3673 (1963).

11 G. Büchi, W.D. Macleod, Jr. and J. Padilla O, J. Am. Chem. Soc., 86, 4438 (1964).

12 E.J. Corey, R.B. Mitra and H. Uda, J. Am. Chem. Soc., 86, 485 (1964).

13 E.J. Corey and S. Nozoe, J. Am. Chem. Soc., 86, 1652 (1964).

14 U. Ramdas Nayak and Salih Dev, Unpublished work.

15 L. Ruzicka and M. Stoll, Helv. Chim. Acta 7, 84 (1924).

16 O. Motl, V. Sykora, V. Herout and F. Sorm, Coll. Czech. Chem. Comm. 23, 1207 (1958).

17 L. Westfelt, Acta Chem. Scand. 18, 572 (1964).

18 M.J.Gallagher, R.P. Hildebrand and M.D.Sutherland, Tetrahedron Letters 40, 3715 (1964).

19 J.D. Briaxo and J. McMurray, J. appl. chem. 2, 187(1952).

20 a) L. Ruzicka and J. Meyer, Helv. Chim. Acta 4, 505(1921)
b) L. Ruzicka, H. Schulz and J. Meyer, ibid. 5, 345(1922)
c) L. Ruzicka and C.F.Siedel, ibid. 5, 363 (1922).

21 W.P. Campbell and M.D.Soffer, J. Am. Chem. Soc., 64, 417 (1942).

22 L. Ruzicka and L. Sternbach, Helv. Chim. Acta 23, 124(1940)

23 V. Herout and V. Sykora, Tetrahedron 4, 246 (1958).

24 J. Krepinsky and V. Herout, Coll. Czech. Chem. Comm. 27, 2459 (1962).

25 K. Kafuku, T. Ikeda and Y. Fugita, J. Chem. Soc. Japan 53, 636 (1932). C.A. 27, 280 (1933).

26 V. Herout, T. Kolos and J. Pliva, Coll. Czech. Chem. Comm. 18, 886 (1953).

27 V. Sykora and V. Herout, Coll. Czech. Chem. Comm. 24, 1732 (1959).

28 A.S.Rao, K.L.Kurve, K.K.Chakravarty and S.C.Bhattacharyya, Tetrahedron 19, 233 (1963).

29 O. Motl and V. Lukes, Coll. Czech. Chem. Comm. 27, 987 (1962).

30 V. Herout and S.I.Dimitrov, Chem. Listy 46, 432 (1952).

31 F. Sorm, M. Holub, V. Sykora, J. Mleziva, M. Streibl, J. Pliva, B. Schneider and V. Herout, Coll. Czech. Chem. Comm. 18, 512 (1953).

32 V.A. Pentegova, O. Motl and V. Herout, ibid. 26, 1362 (1961).

33 a) Jarl Runeberg, Acta. Chem. Scand. 15, 721 (1961).
b) J. B.son Bredenberg, ibid. 15, 961 (1961).

34 This thesis, Part II, Chapter II, p.

35 V. Herout and F. Santavy, Coll. Czech. Chem. Comm. 19, 118 (1954).

36 J. Pliva, V. Herout, B. Schneider and F. Sorm, Coll. Czech. Chem. Comm. 18, 500 (1953).

37 A. Penfold, J. Proc. Roy Soc. N.S.W. 61 337 (1927).

38 R.P. Hildebrand and M.D.Sutherland, Aust. J. Chem. 12, 678 (1959).

39 F. Sorm, V. Herout and V. Sykora, Perf. and ess.oil Rec. 50, 679 (1959).

40 M.D. Soffer, G.E.Gray, D. Korman and M.B. Adams, Tetrahedron letters 5, 389 (1963).

41 Amich Dev and P.C.Guha, J. Indian Chem. Soc. 26, 263(1949).

42 K.K. Chakravarti and B.C.Bhattacharyya, Per. and Ess.Oil Rec. 365 (1955).

43 B.B.Bhatgey, R.K. Razdan and B.C.Bhattacharyya, ibid. 157 (1956).

44 C.C.Kartha, P.S. Kalsi, A.M. Shaligram, K.K.Chakravarti and B.C.Bhattacharyya, Tetrahedron 19, 241 (1963).

45 Dyson, Perf. and Ess. Oil Rec. Jpl No.6 (1936).

46 P.A. Plattner and R. Markus, Helv. Chim. Acta 25, 1674 (1942).

47 G. Kritchevsky and A.B. Anderson, J. Am. Pharm. Assoc. Sci.ed. 44, 595 (1955).

48 H. Erdtman and H. Norbroggen, Acta. Chem. Scand. 14, 2161 (1960).

49 V. Rudloff, Chem. and Ind. 748 (1962).

50 M.D.Soffer, M. Brey and J. Fournier, J. Am. Chem. Soc., 81, 1678 (1959).

51 H. Erdtman, Z. Pelchowicz and J.G. Topliss, Acta. Chem. Scand. 10, 1563 (1956).

52 Jarl Runeberg, ibid. 14, 1991 (1960).

53 K.T. Wang and B. Weinstein, Experientia 19, 519 (1963).

54 a) G. Chiurdoglu, R.R.Snolders and A. Soquet, Bull. Soc. Chem. Belges. 70, 468 (1961).
b) R.R.Snolders, Canad. J. Chem. 42, 2836 (1964).

55 V. Vonasek, V. Herout and F. Sorm, Coll. Czech. Chem. Comm. 25, 913 (1960).

56 M.G. Dauben, B. Weinstein, P. Lin and A.B. Anderson, Tetrahedron 15, 217 (1961).

57 T. Sakai, K. Nishimura, H. Chikamatsu and Y. Hirose, Bull. Chem. Soc. Japan 36, 1261 (1963).

58 V. Herout, J. Hotl and F. Sorm, Coll. Czech. Chem. Comm. 19, 990 (1954).

59 K. Kafuku and H. Kato, Bull. Chem. Soc. Japan 6, 65 (1931).

60 T. Irie, K. Yamamoto and T. Masamune, Bull. Chem. Soc. Japan, 37, 1053 (1964).

61 M.D. Soffer, C. Steinhardt, G. Turner and M.E. Stebbins, J. Am. Chem. Soc., 66, 1520 (1944).

62 S. Katsura, J. Chem. Soc. Japan 63, 1470 (1942).

63 S.C. Bhattacharyya, K.K. Chakravarti and K.L. Kurve, Chem. and Ind. 1352 (1959).

64 R.E. Corbet and W.G. Manger, J. Chem. Soc. 1179 (1954).

65 S.N. Dhingra, J.R. Dhingra and S.C. Bhattacharyya, Perf. and Ess. Oil Rec. 47, 315 (1956).

66 J. Hotl, V. Herout and F. Sorm, Coll. Czech. Chem. Comm. 25, 1656 (1960).

67 L. Dolejs, V. Herout and F. Sorm, Ibid. 26, 811 (1961).

68 W. Triebs, Ber. 82, 530 (1942).

69 F. Sorm, K. Veres and V. Herout, Coll. Czech. Chem. Comm. 18, 196 (1953).

70 P.S. Kalsi, K.K. Chakravarti and S.C. Bhattacharyya, Tetrahedron 19, 1073 (1963).

71 F.H. Couchman, A.R. Pinder and in part N.H. Bromham, Tetrahedron 20, 2037 (1964).

72 L. Ruzicka, J.R. Koolhas and A.H. Wind, Helv. Chim. Acta, 14, 1171 (1931).

73 A. Rinker, J. Volvoda, D. Arigoni, A. Furst, O.Jeger, A.A. Gold and R.B. Woodward, J. Am. Chem. Soc., 76, 313 (1954).

74 V. Sykora, V. Herout and F. Sorm, Coll. Czech. Chem.Comm. 80, 3992 (1958).

75 F. Hanic, ibid. 23, 1751 (1958).

76 C. Djerassi and D. Marshall, J. Am. Chem. Comm. 80, 3992 (1958).

77 P. Baumann and V. Prelog, Helv. Chim. Acta 41, 2362(1958).

78 a) A. Freiga and L. Leskine, Arkiv. Kemi Mineral Geo, B.19 (1944).
b) K. Freudenberg and W. Lwowski, Liebigs Ann. 587, 213 (1954).

79 L. Ruzicka, Experientia, 3 357 (1953).

80 K. Folkers, C.H. Shunk, B.O. Linn, F.M. Robinson, P.E. Wittreich, J.W. Huff, J.L. Gilfillan and H.R.Skeggs, Ciba Foundation Symposium on the Biosynthesis of Terpenes and Sterols (Edited by G.E.W.Wolstenholme and M.O'Connor) p.20, J and A Churchill Ltd., London (1959).

81 J.B. Hendrickson, Tetrahedron 7, 82 (1959).

82 P. de Mayo, J.R.Robinson, D.Y. Spencer and R.W.White, Experientia 18, 353 (1962).

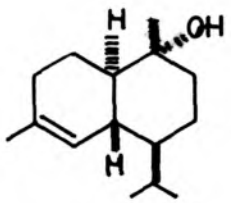
CAPTER II

SYNTHESIS OF METHYLCADALENES

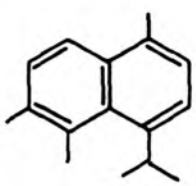
SYNTHESIS OF METHYLCADALENES

Methylcadalenes[1,2] constitute important reference substances for the structure elucidation of cadalenic sesquiterpenoids. The sesquiterpenoid is labelled with an extra-methyl group at the site of a functional group and the product after dehydrogenation gives a methylcadalene. The method has been used for locating the nuclear double bonds[1,3,13] as well as the secondary hydroxyl groups[14] in cadalenic sesquiterpenes. The scope and limitations of this method have been discussed[15] and a modified procedure for labelling the nuclear double bonds by isomerisation of the epoxide with borontrifluoride-etherate and followed by the reaction of the resulting ketone with methyl lithium, reported[15].

There are five theoretically possible methyl cadalenes and the synthesis of all of these have been reported[1,2]. The products were characterised by the preparation of suitable complexes with polynitro compounds. In connection with the structure determination[3] of 4-cadinol (I) it was observed that whereas the picrate, styphnate and the trinitrotoluene complex of 5-methyl cadalene (II) obtainable from 4-cadinol



I



II

were identical with those from the synthetic product, the trinitrobenzene complex of the synthetic product was found to be, in fact, only the complex of 1,2,5-trimethylnaphthalene; apparently the isopropyl group had been eliminated during the last stage of the synthesis, viz. dehydrogenation. On an examination of the laboratory records it was found that whereas the picrate, styphnate and the trinitrobenzene complex had been obtained from a preparation of 5-methylcadalene in which sulphur dehydrogenation was employed at the last stage, the trinitrobenzene complex had been obtained from a preparation in which selenium-dehydrogenation had been used in the last step. The elimination of non-angular alkyl groups during dehydrogenations, though unsuspected at that time, are well established now[16,17], especially for selenium-dehydrogenation. Since selenium dehydrogenation[2] has been employed during the synthesis of several of these methylcadalenes, it was thought desirable, in view of the importance of methylcadalenes as reference substances, to check the structure of these compounds by the modern methods of spectroscopy. However, since the samples on hand were inadequate for the purpose, it was decided to synthesise all the five methylcadalenes afresh, and the occasion has been utilised to introduce new and simpler synthesis of these, except for 5-methylcadalene which was prepared essentially by the procedure already reported[2].

2-Methylcadalene

The procedure followed for the synthesis of 2-methylcadalene is outlined in Fig.1.

The acylation of 2-methyl-p-cymene (IV) could take place at C_5 or C_6 or both depending on the relative importance of electronic or steric factors. In case, substitution occurred preferentially at C_6 (steric factors), the product from the acylation of methyl-cymene with methylsuccinic anhydride would be formulated as VII which could be readily converted into 2-methylcadalene. However, the product from this reaction on oxidation furnished only pyromellitic acid (VIa), hence the keto acid must be assigned the structure V. . This preference for substitution at C_5 was subsequently made use of for the synthesis of 2-methylcadalene as shown in Fig.1. The compound has been previously synthesised by Soffer et al.[1].

3-Methylcadalene*

3-Methylcadalene has been prepared following the scheme outlined in Fig.2. Its previous synthesis was reported by Sukh Dev[2].

As anticipated from the previous work on the synthesis of 2-methylcadalene, the acylation of 3-methyl-p-cymene with methyl succinic anhydride yielded the required compound, the structure of which was proved by its oxidation to pyromellitic acid (VIa). A point of special interest in this

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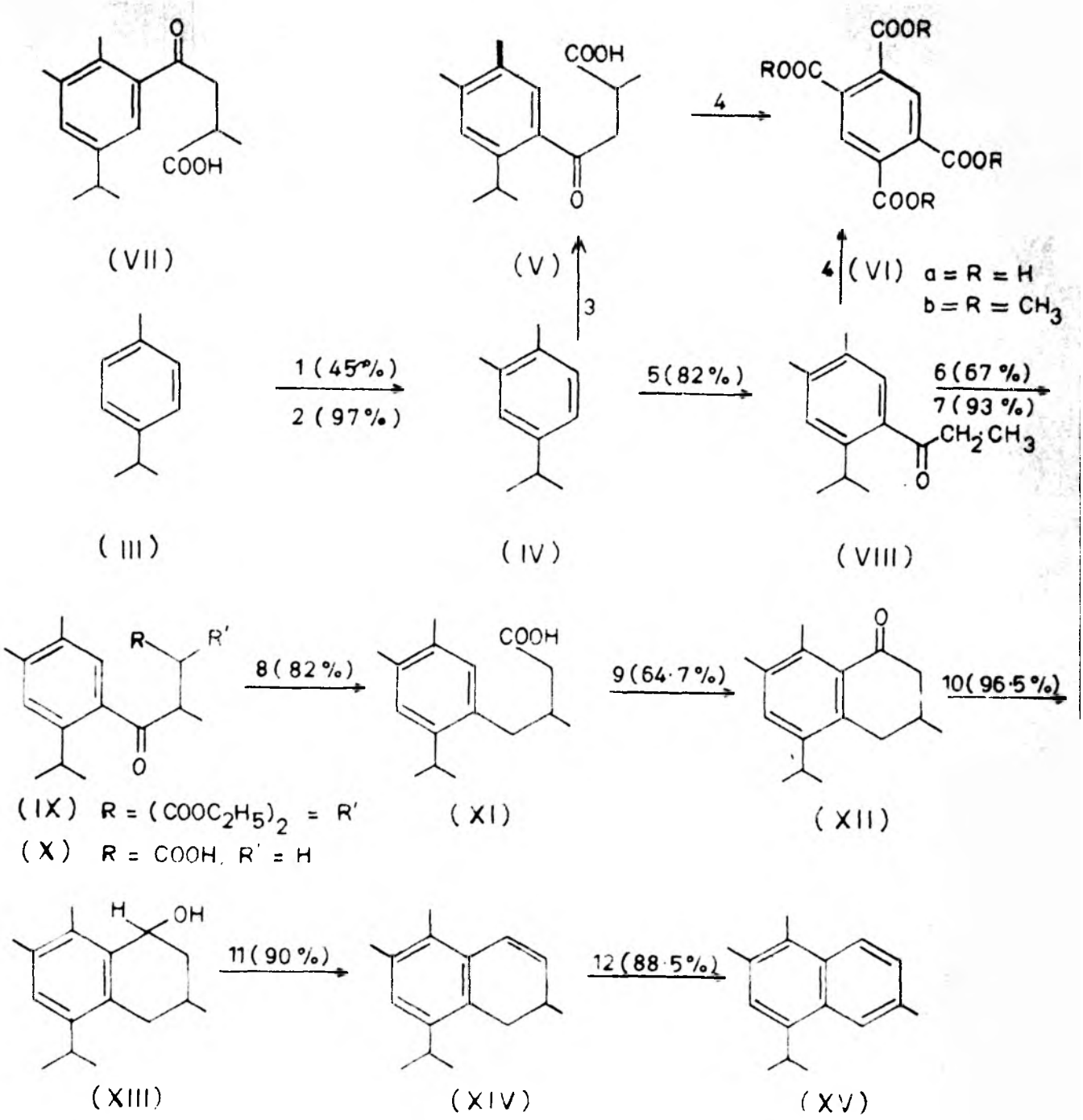
*With Charanjit Rai.



REAGENTS —

1 HCHO , HCl
2 H_2, Pd - C
3 Methylsuccinic anhydride
4 HNO_3
5 CH_3CH_2COCl, $AlCl_3$
6 Br , diethyl malonate
7 Hydrolysis
8 Zn - Hg, HCl
9 PPA
10 $LiAlH_4$
11 I_2
12 Sulphur

FIG 1 : SYNTHESIS OF 2-METHYLCADALENE

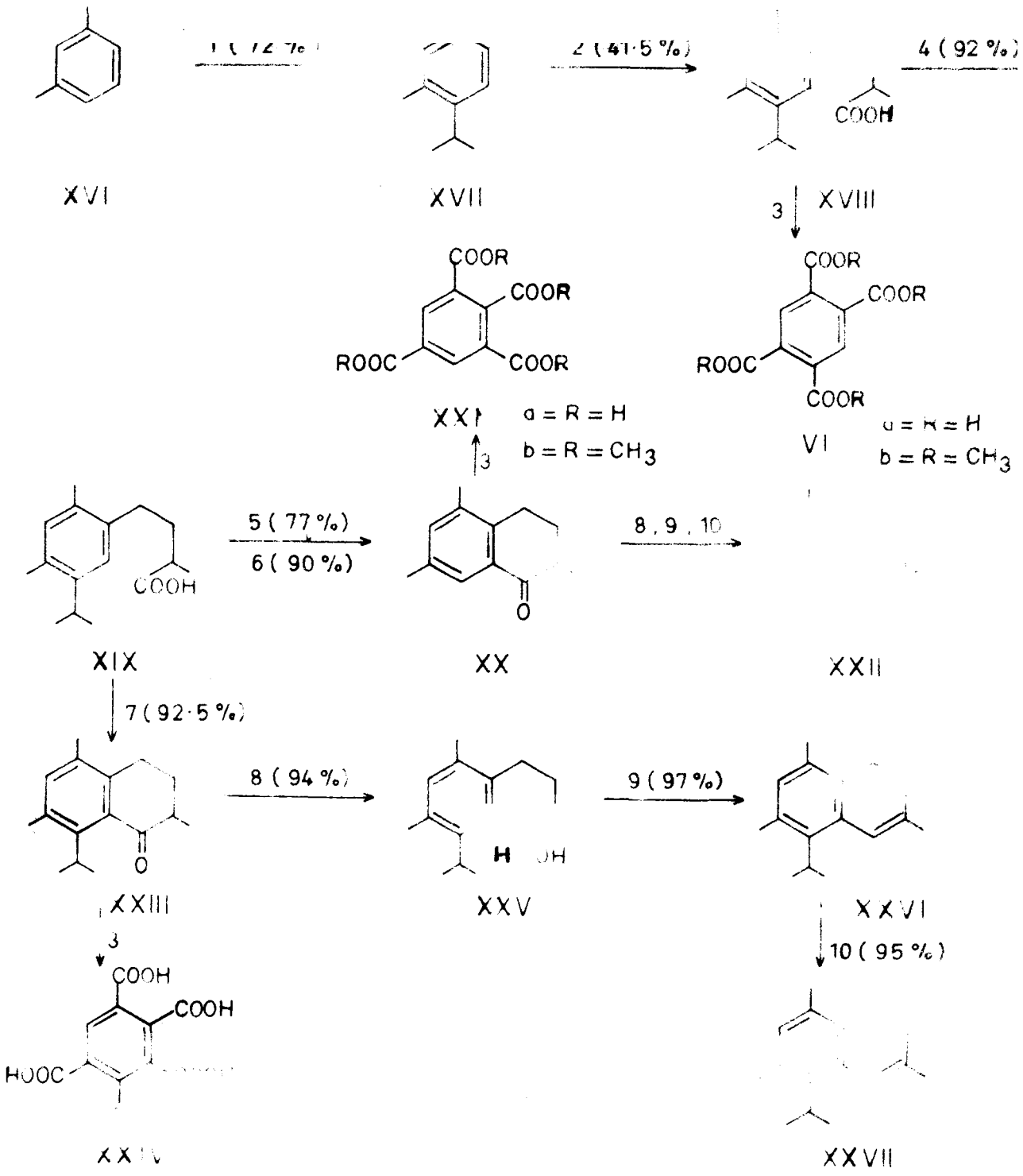


FIG. 2 · SYNTHESIS OF 3-METHYLCADALENE

work has been that the action of polyphosphoric acid on the acid XIX, or the action of Aluminium chloride on the acid chloride of the acid XIX furnished only 2,5,7-trimethyltetralone-1 (XX) rather than the expected 2,5,7-trimethyl-8-isopropyl-tetralone-1 (XXIII); the tetralone XX was duly characterised by its oxidation to mellophanic acid (XXI) and its conversion to 1,3,6-trimethylnaphthalene (XXII). Though dealkylations[18,19,20] and rearrangement of alkyl groups is a recognised feature in certain Friedel-Crafts reactions, not many cases of dealkylations appear to have been recorded for the intramolecular ring-closure reactions.*

5-Methylcadalene

This was prepared according to the method of Sukh Dev[2] with suitable modifications (Fig.3).

7-Methylcadalene**

7-Methylcadalene was obtained by following the scheme outlined in Fig.4. This method is far simpler than the route followed by previous workers[1].

8-Methylcadalene

8-Methylcadalene was synthesised following the

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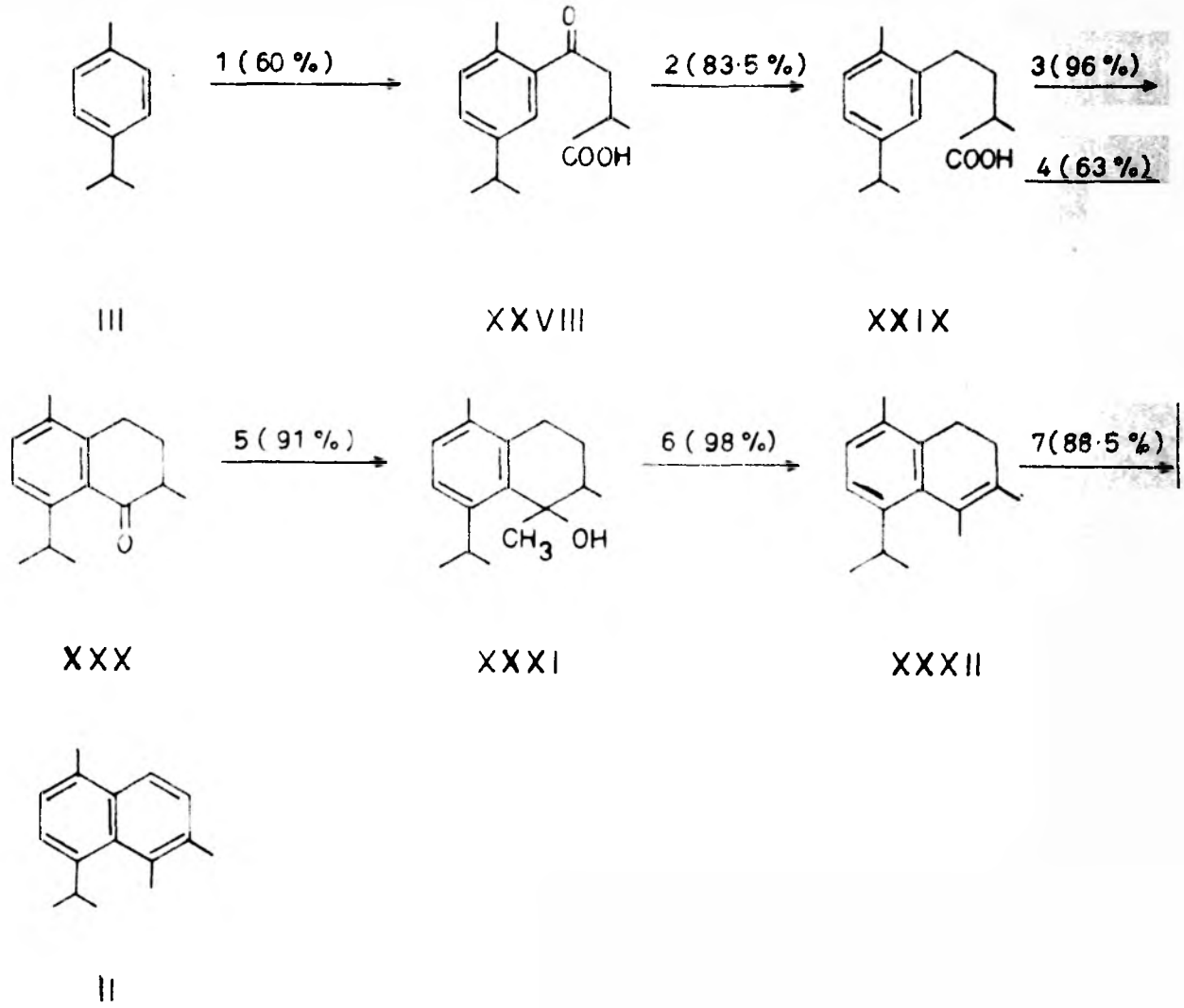
*For example, in the chapter on "The formation of cyclic ketones by intramolecular acylation" by W.S.Johnson in Organic Reactions (Edited by Roger Adams), Vol.II, pp.114, John Wiley and Sons, New York (1946) which covers the literature upto 1945 no such cases have been reported.

The cleavage of a t-butyl group during intramolecular ring-closure of γ(2-methyl-4-t-butylphenyl)-butyric acid, has been reported[21].

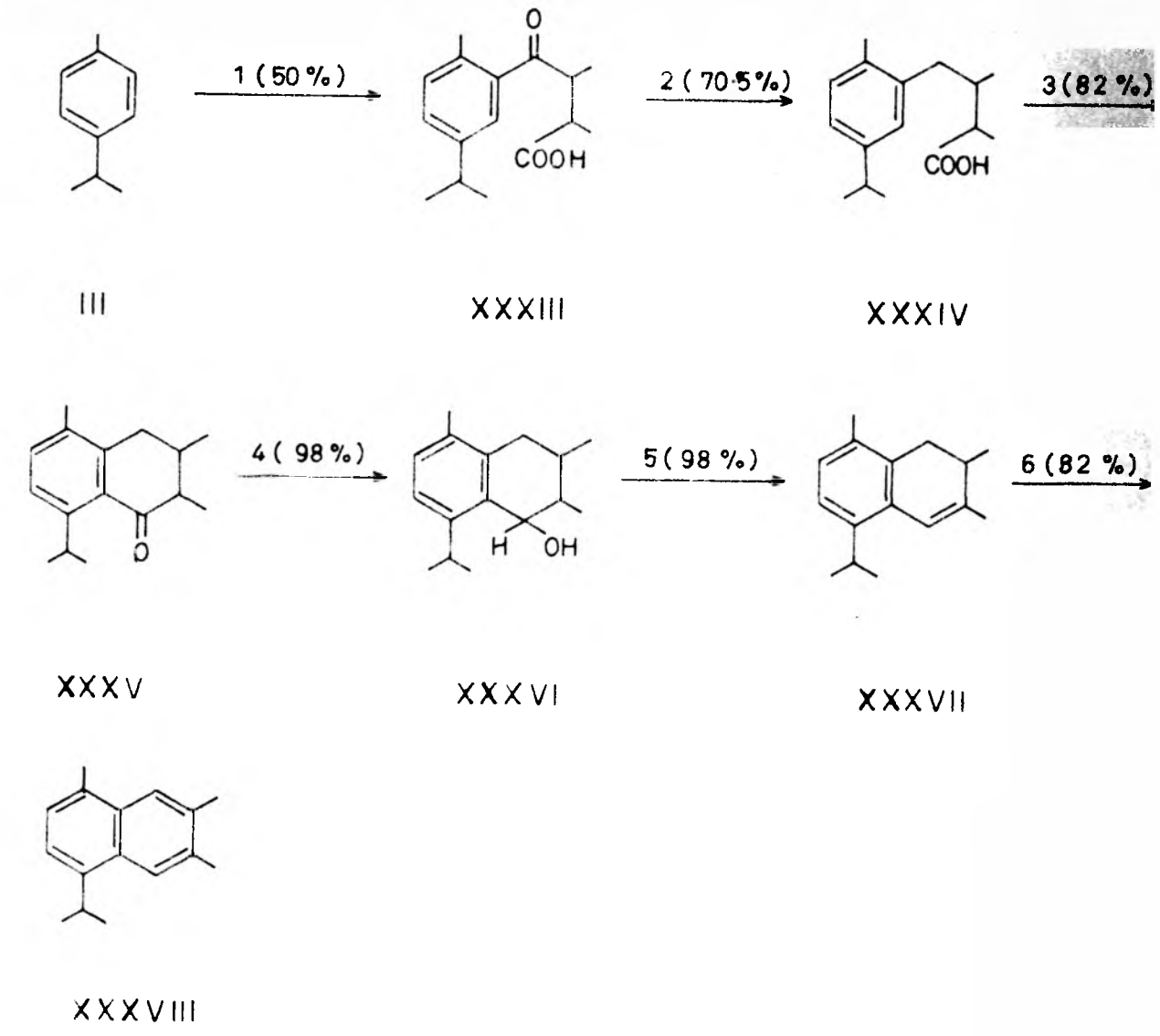
**With K.L. Murthy.



REAGENTS —

1 Methyl succinic anhydride, $AlCl_3$
2 Zn-Hg, HCl
3 PCl_5, $AlCl_3$
4 PPA
5 Methyl-lithium
6 I_2
7 Sulphur

FIG. 3 SYNTHESIS OF 5-METHYCADALENE



III XXXIII XXXIV

XXXV XXXVI XXXVII

XXXVIII

REAGENTS –

1 Dimethyl succinic anhydride $AlCl_3$
2 Zn-Hg, HCl
3 PPA
4 $LiAlH_4$
5 I_2
6 Sulphur

FIG 4 : SYNTHESIS OF 7-METHYLCADALENE

procedure shown in Fig.5. The first synthesis of 8-methylcadalene was reported by Sukh Dev[2].

In connection with the reduction of the acid XXXIX and the lactoneXL with hydriodic acid and red phosphorous, it may be pointed out that the formation of a tetralone during such reactions has been reported earlier[22,23,24]

1,2,7-Trimethyl-4-isopropylnaphthalene

The fact that the acylation of 2-methyl-p-cymene with methyl succinic anhydride yielded the keto acid (Fig.1), was utilised to prepare (Fig.6), 1,2,7-trimethyl-4-isopropylnaphthalene which was thought to be of interest in connection with the nuclear magnetic resonance (NMR) studies[25] of alkylnaphthalenes.

SOME GENERAL REMARKS:

In all of these syntheses, the final step of dehydrogenation was carried out with sulphur in order to avoid the loss of alkyl groups during dehydrogenation. In order to make this reaction more facile, the tetralones were converted to the corresponding alcohols which were dehydrated with iodine[26] to give the corresponding dialins in excellent yields, which in turn could be smoothly dehydrogenated to the required naphthalenes.

The ultraviolet and the infrared data of the various tetralones obtained during this work are summarised in Table 1. As can be seen no special comments are called for the ultraviolet absorption data which fall within the

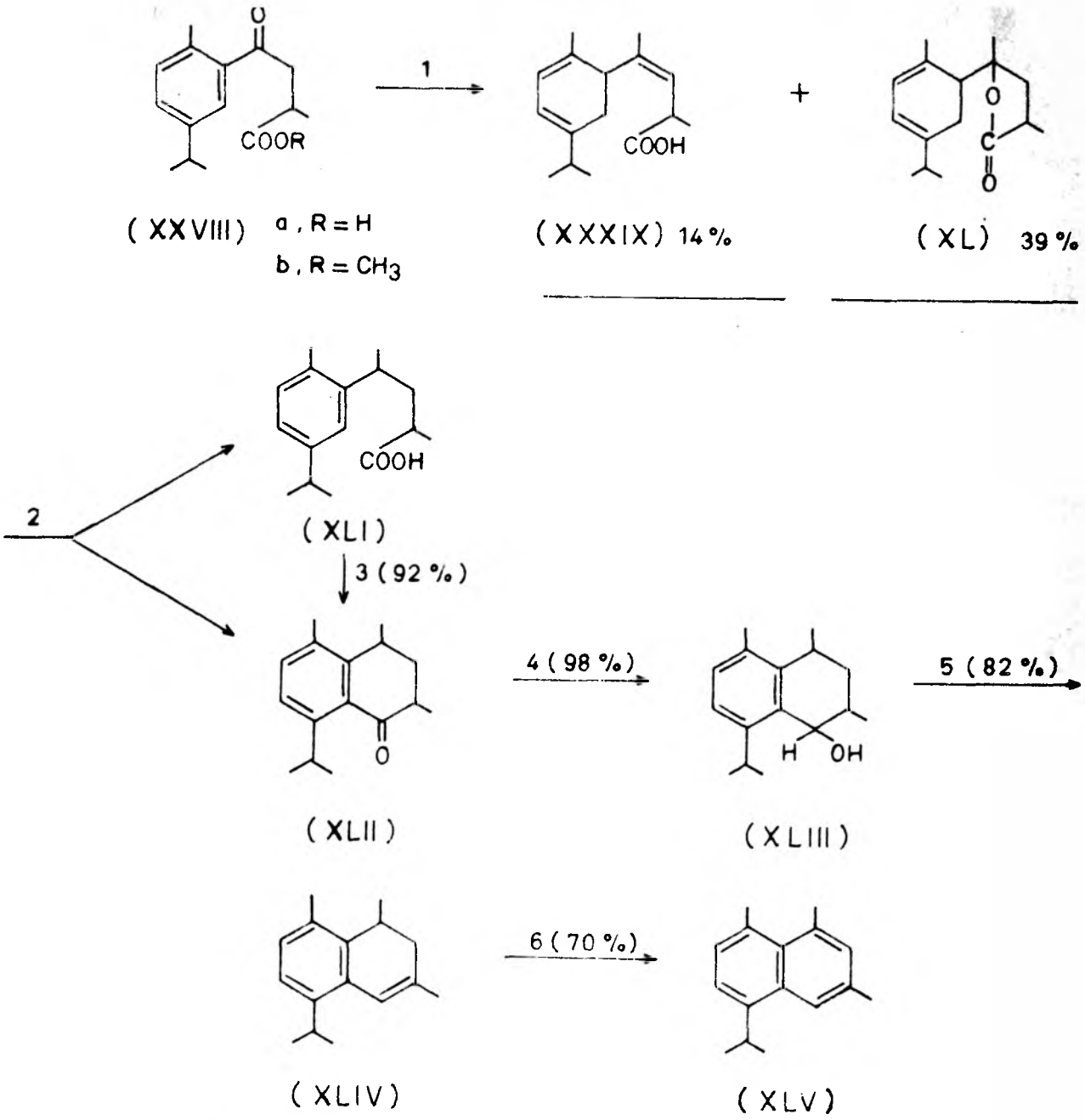
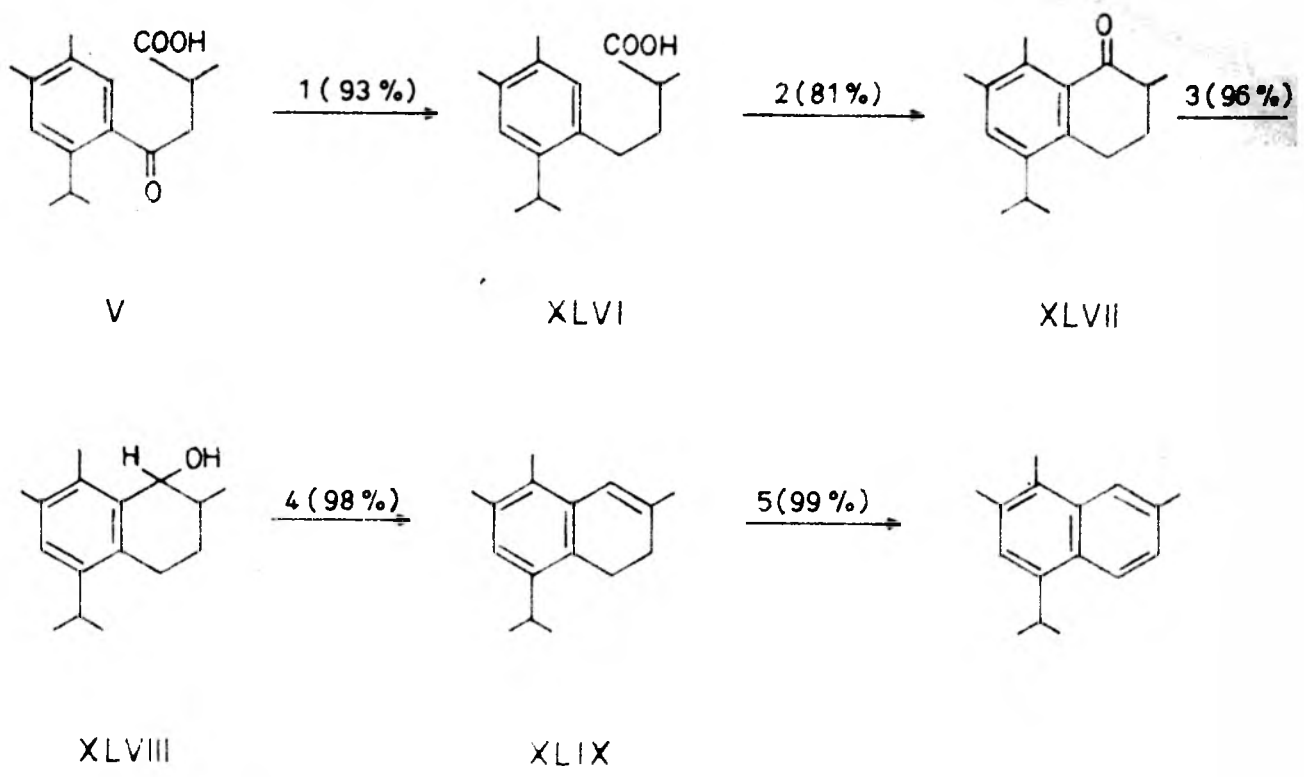


FIG. 5. SYNTHESIS OF 8-METHYLCADALENE



REAGENTS –

1 Zn–Hg, HCl

2 PPA

3 $LiAlH_4$

4 I_2

5 Sulphur

FIG. 6 SYNTHESIS OF 1,2,7-TRIMETHYL-4-ISOPROPYLNAPHTHALENE

TABLE 1: UV AND IR SPECTRAL DATA OF VARIOUS TETRALONES

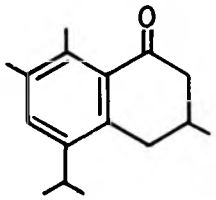
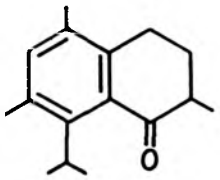
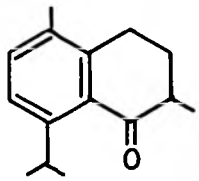
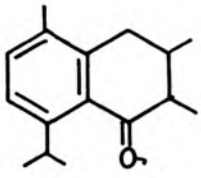
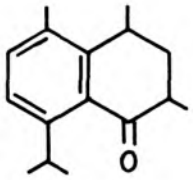
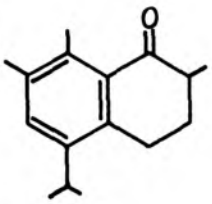
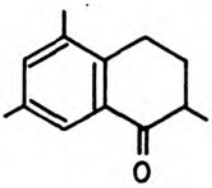
No.	Tetralone	Ultraviolet absorption.		Infrared absorption.	
		ethanol λ_{max}, mμ	ε_{max}	$\nu^{c=o}$, cm^{-1}	Other important bands cm^{-1}
I		305 257.7 214	4274 10160 26050	1667	889 938 1005
II		303 257 220	2050 8213 24000	1689 1678	823 880 982
III		302 253 217	2134 9475 21440	1681	828 847 891 965
IV		300 251.6 217	1643 7645 19770	1681 1783	827 988
V		301 254 218.5	2428 9055 21090	1678	840 889 989

TABLE 1 (Contd.)

No.	Tetralone	U.V. absorption		I.R. absorption	
		$\lambda_{max}^{ethanol}$, mμ	ε_{max}	$\nu^{c=o}$, cm^{-1}	Other important band cm^{-1}
VI		308 256 214.5	2420 9774 30430	1667	796 891 925 980
VII		3.281 253	1914 10480	1678	721 758 883 907 988

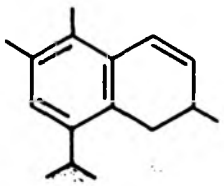
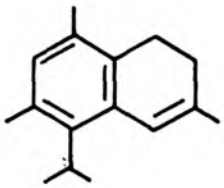
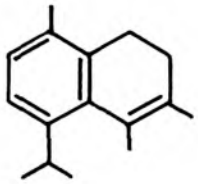
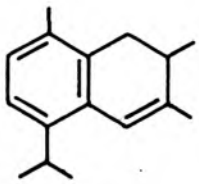
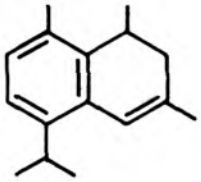
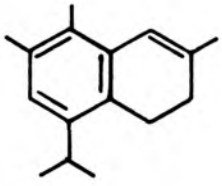
normal expected range[27,28]. The infrared carbonyl stretching frequencies for these tetralones offer some points of interest. Thus, for instance, tetralone I and VI absorb at comparatively lower frequencies as compared to others which fall within the expected range[29] ($\sim$1680 cm^{-1}), however no explanation for this is apparent. It may be further noted that tetralone II and IV display two carbonyl stretching frequencies.

The ultraviolet spectra of the various dialins obtained during this work have been summarised in Table 2. It will be noticed that the spectral data is in accord with the expectations[30]. It may also be pointed out that the slight hypsochromic shift observed in case of II and III (Table 2) might have itsorigin in the slight twisting of the chromophore on account of the overcrowding due to the neighbouring methyl and isopropyl groups.

The physical properties of the various naphthalenes synthesised during this work are summarised in Table 3. The melting points of their complexes with suitable poly-nitro compounds have been collected in Table 4.

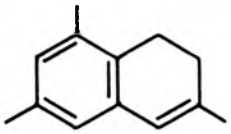
The methylcadalenes obtained during this work yielded derivatives (Table 4) which have been found to be identical with the derivatives described by previous workers [1,2,31] with the exception of the trinitrobenzene complex of 5-methylcadalene[2].

TABLE 2 : ULTRAVIOLET SPECTRAL DATA OF THE DIALINS

No.	Dialin	Ethanol λ_{max}, nm	ϵ_{max}
I		267	11530
		231 (s)*	41260
		225	36370
		219	28480
II		263	15150
		223	50190
III		262	9707
		234	29180
		219	29660
IV		271	12350
		233 (s)*	24710
		225	36530
		219	35180
V		271	12630
		233	25260
		225.5	36110
		218	31760
VI		260	12900
		234 (s)*	20140
		226	34150
		221	33360

Contd...

TABLE 2 (Contd.)

No.	Malin	$\lambda^{Ethanol}_{max}$, mμ	ε_{max}
VII		268	15480
		231 (s)*	36120
		225	51170
		219-225	48150

* s = shoulder.

TABLE 3: PHYSICAL PROPERTIES OF CADALENE, METHYLCADALENES AND SOME OTHER NAPHTHALENIC HYDROCARBONS.

Compound.	m.p.	b.p./mm	d_4^{30}	n_D^{30}	M_D	EM_D	$E\Sigma_D$
Cadalene	-	117-19°/1	0.9690	1.5810	70.52	1.167	0.5833
2-Methylcadalene	-	128-30°/1.5	0.9707	1.5838	72.96	3.6270	1.7070
3-Methylcadalene	-	129-31°/ "	0.9721	1.5840	72.97	3.6170	1.7060
5-Methylcadalene	-	144-45°/ "	0.9847	1.5926	72.86	3.5070	1.6550
7-Methylcadalene	39-40°	139-40°/ "	-	-	-	-	-
8-Methylcadalene	-	135-36°/ "	0.9800	1.5876	72.79	3.3870	1.5980
1,2,7-Trimethyl-4-isopropylnaphthalene.	59-60°	139-40°/ "	-	-	-	-	-
1,3,6-Trimethyl-naphthalene.	-	119-20°/ "	0.9956	1.5976	58.19	2.6910	1.5830

TABLE 4 : DERIVATIVES OF METHYLCADALENES AND THEIR MELTING POINTS.

Methylcadalene	TNB Complex		TNT Complex	
	Present sample	Reported	Present sample	Reported
2-Methylcadalene	169-70°	168.5-69°[1]	118-20°	-
3-Methylcadalene	162-63°	165°[2]	97-98.5°	-
5-Methylcadalene	112-13.5°	160-61°[2]	86-87.5°	87-88°[2]
7-Methylcadalene	126-27°	-	72.73°	-
8-Methylcadalene	116-17°	118-18.5°[2] 117.5°[31]	45-64°*	56-61°[31]

*The complex is unstable.

EXPERIMENTAL

All m.ps. and b.ps. are uncorrected. Pet.ether refers to the fraction b.p. 40-60°. All solvent extracts were finally washed with brine before drying (Na_2SO_4).

UV spectra were taken on a Beckman DK-2 Ratio Recording Spectrophotometer. IR spectra were taken on both Perkin-Elmer Spectrophotometer model 221 and Perkin-Elmer Infracord model 137-E either as smears (liquid) or in nujol (solids).

Alumina used for chromatography was made neutral by CO_2 method[32] and standardised according to Brockmann[33].

2-METHYLCADALENE

2-Methyl-p-cymene (IV)

(i) Chloromethylation of p-cymene: A mixture of p-cymene III (purified by H_2SO_4 method and distilled over Na, 92 g), para-formaldehyde (40 g), glacial acetic acid (90 ml), syrupy phosphoric acid (60 ml) and conc. HCl (135 ml) was taken in a suitable 3-necked flask and stirred vigorously at 100° ± 2 for 7 hr. The reaction mixture was cooled, diluted with ice-cold water (120 ml) and the upper hydrocarbon layer separated. The aqueous part was extracted with ether (50 ml x 4), the combined hydrocarbon layer and ether extracts were washed with water and dried. The solvent was flashed off and the residue fractionated to give the required 2-chloromethyl-p-cymene*

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*Contaminated with 3-isomer.

b.p. 138-40°/15 mm, $n_D^{26.5}$ 1.5220, yield 56.420 g (45.03%) Lit.[34]: b.p. 123-24°/20 mm) (unreacted p-cymene distilled as the fore-run, b.p. 93°/35 mm, wt. 36.5 g).

(ii) Hydrogenolysis of 2-chloromethyl-p-cymene: The above 2-chloromethyl-p-cymene (55 g) in ethanol (95%,200 ml) was shaken in presence of 10% Pd-c (3.0 g) for 8 hr in an atmosphere of hydrogen (hydrogen consumed:28°/720 mm,8.774 litre). The catalyst was filtered off, washed with pet. ether (50 ml x 4), water added (200 ml) to the filtrate and the solvent layer separated. The aqueous part was extracted with pet. ether (100 ml x 4), the combined extracts washed with water and dried. The solvent was removed and the residue fractionated to yield 2-methyl-p-cymene, b.p. 111-12°/40 mm, n_D^{23} 1.5000, yield 43.280 g (97%). (Lit.[35]: b.p. 86-87.5°/16 mm, $n_D^{21.1}$ 1.4991).

α-Methyl-β-(3,4-dimethyl-6-isopropylbenzoyl)-propionic acid(V):

To an intimate mixture of 2-methyl-p-cymene (IV; 19.6 g, 1.1 mol), methylsuccinic anhydride (12.8 g, 1 mol) and nitrobenzene (freshly distilled, 75 ml), chilled at -5°, anhydrous Aluminium chloride (35.2 g, 2.2 mol) was added in 4 lots during 2 hr with vigorous stirring. The stirring was continued further for 3 hr and the reaction mixture left overnight (28°). The syrupy complex was chilled and treated with crushed ice (100 g) and conc. HCl (30 ml). The product was allowed to stand for one hr and was extracted with ether (50 ml x 5). The combined ether extracts were

washed with HCl (25 ml), water (50 ml x 3) and extracted with aq. NaOH (5%, 50 ml x 4). The alkaline extract was boiled with norite for 2 hr, filtered hot, the filtrate cooled and acidified with dil HCl (congo red). The liberated acid was initially gummy in nature but solidified on standing (4 days), m.p. 55-60°, yield 27.0 g (77.8%). It crystallised from dil. acetic acid and an analytical sample had m.p. 72.5-73.5° (Found: C, 77.67; H, 8.54. $C_{16}H_{22}O_3$ requires: C, 77.25; H, 8.45%).

From the mother liquors an acid m.p. 131-33°, yield 2.5 g (10%), was obtained. Mixed m.p. with 4-methyl-3-(2,4-dimethyl-5-isopropylbenzoyl)-propionic acid (XVIII) remained undepressed.

The above keto acid (V, 0.2 g) was mixed with dil. nitric acid (1 ml con. HNO_3 and 2 ml H_2O) and heated in a sealed Carius tube at 190-200° for 15 hr[36]. The product was evaporated to dryness and made free from HNO_3 by repeated evaporation with water. The residue (0.115 g) was treated with a slight excess of diazomethane and the resulting methyl ester crystallised from methanol, m.p. 141-42.5°, (Lit.[1] gives the m.p. 142-43.5° for the tetramethyl ester of pyromellitic acid, VIb) yield, 0.050 g (Found: C, 54.82; H, 4.89. $C_{14}H_{14}O_8$ requires: C, 54.2; H, 4.55%).

3,4-Dimethyl-6-isopropylpropiophenone (VIII):

Anhydrous $AlCl_3$ (35 g, 2 mol) was added in two lots to nitrobenzene (freshly distilled, 45 ml), placed in a 3-necked

flask and mechanically stirred. When all the $AlCl_3$ had dissolved the flask was chilled to 0° and the $AlCl_3$-nitrobenzene complex separated out. A mixture of 2-methyl-p-cymene (IV; 19.150 g, 1 mol) and propionylchloride (12 g, 1 mol) was then introduced in the flask containing $AlCl_3$-nitrobenzene complex, dropwise,(45 minutes) maintaining the temperature below 10°. The reaction mixture was left as such overnight (~ 20°) and then was treated with crushed ice (100 g) and conc. HCl (30 ml). The oil was extracted with ether (50 ml x 4), the combined ether extracts were washed with conc. HCl (25 ml), water and dried. The solvent was flashed off and the residue fractionated to give the required ketone VIII, b.p. 144-45°/12 mm, n_D^{25} 1.5180, yield 20.080 g (80.47%) (Found: C, 82.9; H, 10.2. $C_{14}H_{20}O$ requires: C, 82.35; H, 9.8%). IR spectrum: $\nu^{C=O}$ 1678 cm^{-1}.

The 2,4-dinitrophenylhydrazone prepared from the ketone (0.2 g) by diglyme method[27] crystallised from ethanol, m.p. 131-32.5°.

The above ketone (VIII; 0.44 g) was mixed with dil. HNO_3 (2 ml conc. HNO_3 and 4 ml H_2O) and heated in a sealed Carius tube at 190-200° for 15 hr. The product was diluted with water and evaporated,and the process repeated till the residue was free from HNO_3. The acid (0.320 g) thus obtained was treated with diazomethane and the resulting methyl ester crystallised from methanol, m.p. 136-40°, yield 0.21 g. Mixed m.p. with authentic sample of VIb remained undepressed.

2-methyl, 3-(3,4-dimethyl-6-isopropylbenzoyl)-propionic acid (X).

(i) Bromination:

The above ketone (VIII; 10 g, 1 mol) in dry ether (10 ml) was chilled to 0° and to it was added a trace of $AlCl_3$ and then bromine (2.9 ml, 1 mol) in 1 ml portions. Decolourisation was quite rapid and when the reaction was complete, ether and HBr were removed immediately under suction, in a thin current of dry air. The syrupy liquid residue was used as such in the next step.

(ii) Condensation of the above bromoketone with sodium Malonate:

Sodium (2.420 g, 1 A) was powdered under dry xylene (50 ml) which was then replaced by dry toluene (50 ml). Diethylmalonate (17 g, 1 mol) was added dropwise (40 minutes) to the Na-dust and the Na-salt which formed instantaneously was refluxed at 130-40° for 2 hr. To the cold Na-salt of the diethylmalonate the above bromoketone was added dropwise and the whole mixture was then refluxed for 10hr. The product was acidified slightly and steam-distilled to remove the unreacted malonic ester. The residue was taken up in ether (50 ml x 3), washed with water and the solvent flashed off to give the crude diester (IX; 11.700 g) (67.57%) which was hydrolysed with alcoholic NaOH (15%, 100 ml). The usual work up gave the required keto acid X, as a brown solid, m.p. 112-24°, yield 8.1 g (93.33%).

An analytical sample had m.p. 142-43.5°. (Found: C, 73.13; H, 8.65. $C_{16}H_{22}O_3$ requires: C, 73.25; H, 8.45%).

2-Methyl-4-(3,4-dimethyl-6-isopropylphenyl)-butyric acid (XI):

The crude keto acid (X; 10.0 g) was reduced with Zinc-amalgam (from 20 g Zn wool, 2 g $HgCl_2$, 3 ml HCl conc. and 40 ml H_2O) and dil HCl (56 ml conc. HCl, 27 ml H_2O) with the addition of toluene (35 ml) and glacial acetic acid (4 ml) by refluxing the whole mixture at 130-40° for 36 hr. After every six hr, con. HCl (15 ml) was added. The reaction mixture was cooled, toluene layer separated, washed with water and dried. The solvent was removed and the residue distilled to yield the required acid XI as a colourless, viscous liquid, b.p. 152-55°/0.5 mm, n_D^{25} 1.5186, yield 7.8 g (82.33%) (Found: C, 77.10; H, 9.61. $C_{16}H_{24}O_2$ requires: C, 77.37; H, 9.74%).

2,3,7-Trimethyl-5-isopropyltetralone-1 (XII):

The above acid (4 g) was added all atonce with swirling to PPA (from 20 g P_2O_5 and 12 ml syrupy H_3PO_4) kept at 97°C. The whole mixture was maintained at 97° for 1/2 hr with occasional stirring (3 minutes at the interval of 10 minutes). The reaction product was poured onto ice (50 g) and extracted with a mixture of pet. ether: ether (1:1) (25 ml x 4). The combined extracts were washed with water (20 ml x 2), aq. Na_2CO_3 (5%, 10 ml x 2), finally with water (20 ml x 3) and dried. The solvents were flashed off and the residue fractionated

to yield the tetralone XII as a pale yellow oil which solidified immediately, b.p. 142-55°/1.5 mm, m.p. 44-60°, yield 3.0 g. By repeating the above experiments a total of 12.5 g (m.p. 44-60°) of the above tetralone was collected. As the purification of the tetralone by crystallisation was found to be rather difficult, hence it was achieved by chromatographing 10.5 g of the tetralone over Al_2O_3/I (185 g, 24 cm x 3 cm).

Frac.1:	Pet.ether	15 x 200 ml	7.1150 g	m.p. 62-70°
Frac.2:	Benzene	1 x 200 ml	1.1015 g	" 49-54°
Frac.3:	Benzene	2 x 200 ml	0.3001 g	" 79-85°
Frac.4:	Benzene	4 x 200 ml	0.200 g	" 50-82°

Fraction 1 was crystallised to a constant m.p. 69.5 - 70.5° and it analysed for $C_{16}H_{22}O$ (wt. 6.0 g, 64%). (Found: C, 83.79; H, 9.71. $C_{16}H_{22}O$ requires: C, 83.43; H, 9.63%). $\lambda_{max}^{ethanol}$ 305 mμ ε 257.7, 214 mμ ε, 2274, 10160, 26050. IR : $\nu^{C=O}$ 1667 cm^{-1}.

<u>1,2,6-Trimethyl-4-isopropyl-5,6-dihydronaphthalene (XIV)</u>:

<u>$LiAlH_4$ reduction</u>: $LiAlH_4$ (0.495 g, 1.5 mol) was placed in a 250 ml conical flask, fitted with a condenser and a dropping funnel, and covered immediately with dry ether (80 ml). The flask was chilled to ~-5° and the contents stirred magnetically to make a uniform slurry to which the above tetralone (2.0 g, 1 mol) was added slowly (15 minutes) with vigorous stirring which was continued for a further period of 2 hr. The reaction product was left overnight and was then treated at ~0°

with ice-cold water (30 ml) followed by aq. Rochelle salt (40%,75 ml). The solvent layer was removed and the aq.part extracted with ether (30 ml x 4). The combined extracts were washed with water (25 ml x 3) and dried. The solvent was removed under suction at room temperature (~30°) and the crude carbinol XIII (2.920 g, 36.49%) was used as such in the next step.

Dehydration: The above carbinol (2.920 g) was mixed with iodine (50 mg) and heated on a waterbath at ~95° for 1 hr. The product was taken up in pet. ether (50 ml), washed with water (15 ml x 3), aq. sodiumbisulphite (10%,25 ml x 2), water (15 ml x 2) and dried. The solvent was flashed off and the residue distilled over Na,to furnish the required dialin XIV as a colourless liquid, b.p. 122-24°/2 mm, n_D^{24} 1.5545, yield 2.4230 g (89.95%). (Found: C, 89.4; H, 9.9. $C_{16}H_{22}$ requires: C, 89.65; H, 10.35%) $\lambda_{max}^{ethanol}$ 267, 225, 219 mμ. ε, 11530, 36270, 28480 resp.

2-Methylcadalene (XV)

The above dialin (2.360 g) was mixed with sulphur (0.354) and heated at 205-10°/200 mm for 3 hr. The product was distilled over a pinch of freshly prepared Na. powder, b.p. 131-33°/2 mm, n_D^{24} 1.5792, yield 2.0323 g (88.5%).

Trinitrobenzene derivative: Trinitrobenzene (1.6 g) was dissolved in ethanol (95%,10 ml) and to it was added 2-methylcadalene (2.0323 g) in ethanol (95%,2 ml) and the mixture warmed, to a clear solution. On cooling, the crystals

separated which were filtered/washed with ethanol, and dried. m.p. 166-67.5°, yield 2.70 g. Similarly a total quantity of 3.432 g of the TNB complex was collected from other experiments. An analytical sample of the TNB complex had m.p. 169-70.5° (Lit.[1]: m.p. 168.5-169°) (Found: C, 62.1; H, 5.1; N, 9.87. $C_{22}H_{23}O_6N_3$ requires: C, 62.16; H, 5.45; N, 9.88%).

Pure sample of 2-Methylcadalene: The TNB complex of 2-methylcadalene (m.p. 169-70.5°, 2.9225 g) was passed through a column of basic Al_2O_3/I (120 g, 17 cms x 3 cm) using pet. ether as the eluent. The regenerated hydrocarbon obtained after the solvent removal was distilled over Na, b.p. 128-30°/1.5 mm, n_D^{30} 1.5838, d_4^{30} 0.9707, M_D 72.98, EM_D 3.6270 $E\Sigma_D$, 1.7070.

Trinitrotoluene complex: Trinitrotoluene (TNT) (0.200 g, 1 mol) was dissolved in ethanol (95%,2 ml) and to it was added pure sample of 2-methylcadalene (0.200 g,1 mol) in ethanol (1 ml) and the mixture was warmed till a clear solution was obtained; it was allowed to cool slowly. The compound was removed by filtration and recrystallised twice from 95% ethanol, m.p. 119-20° (Found: C, 62.2; H, 5.8. $C_{23}H_{25}O_6N_3$ requires: C, 62.86; H, 5.73%).

3-METHYLCADALENE

3-Methyl-p-cymene (XVII)

To a mixture of m-xylene (XVI; extra pure, freshly distilled over Na, 374 ml, 334 g) and isopropyl alcohol (48 ml)

placed in a 2 litre three-necked flask maintained at ~ 0°, was added with stirring, dil H_2SO_4 (500 ml conc. H_2SO_4, 110 ml H_2O) during 2 hr and the stirring continued further for 14 hr. The hydrocarbon layer was separated and the aqueous part was extracted with pet. ether (50 ml x 4). The combined extracts were washed with water (50 ml x 4), and dried. The solvent was flashed off and the residue fractionated (unreacted m-xylene distilled as the forerun b.p. 75-80°/75 mm, 2.2 g).

	b.p.	n_D^{28}	Wt.	Total yield.
Frac.1	85°/55 mm	1.4991	2.343 g	
Frac.2	104°/55 mm	1.5000	31.860 g	50.9710 g (72%)
Frac.3	103°/70 mm	1.5013	17.875 g	
Frac.4	108°/55 mm	1.5018	1.2360 g	

(Lit.[38]: b.p. 77/13 mm, n_D^{25} 1.4998, yield 75%).

Fractions 2 and 3 were combined for using in the next step.

<u>β-Methyl-β(2,4-dimethyl-5-isopropylbenzoyl)-propionic acid (XVIII)</u>

A mixture of 3-methyl-p-cymene (XVII; 45 g, 1.1 mol), methyl succinic anhydride (29.0 g, 1 mol) and freshly distilled nitrobenzene (175 ml) were taken in a suitable 3-necked flask and chilled to ~ 5°, to which anhydrous $AlCl_3$ (80 g, 2 mol) was added in 4 lots during 1-1/2 hr, with stirring. The reaction product was worked up in the usual manner and the crude acid (58 g, 72.81%, m.p. 130-30°) obtained was crystallised from benzene:pet. ether mixture (1:2), m.p. 131.5°-33.5°,

yield 33.0 g (41.43%).

The above acid (XVIII; 0.2 g) was oxidised with dil HNO_3 (1 ml HNO_3 and 2 ml H_2O) at 185-90° for 18 hr. The acid obtained (0.15 g) after an usual work up was esterified with a slight excess of diazomethane and the resulting methyl ester crystallised from methanol, m.p. 140-42.5°, yield 0.040 g. Mixed m.p. with an authentic sample of VIb remained undepressed (141.5 - 42.5°).

4-Methyl-4-(2,4-dimethyl-5-isopropylphenyl)-butyric acid (XIX)

The pure keto acid (XVIII; 28 g) was reduced by refluxing with Zn-amalgum (from 65 g Zn-wool, 6.5 g $HgCl_2$, 6.5 ml conc. HCl and 108 ml H_2O), dil HCl (162 ml conc. HCl and 55 ml H_2O), toluene (81 ml) and gl. acetic acid (8 ml) for 36 hr. The usual work up gave the required acid which was purified by distillation, b.p. 163-67°/0.5 mm n_D^{28} 1.5110, yield 24.564 g (92.64%). The acid solidified on standing and crystallised from pet. ether, m.p. 55-59°.

Oxidation of the above acid (XIX; 0.2 g) with dil. HNO_3 (1 ml conc. HNO_3 and 2 ml H_2O) by heating in a sealed Carius tube at 190-200° for 18 hr furnished an acid which was esterified with diazomethane and the ester crystallised from methanol, m.p. 140-41.5°. Mixed m.p. with the authentic sample of VIb remained undepressed (140-42°).

2,5,7-Trimethyl-tetralone-1 (XX):

(i) PPA method: The acid (XIX; 15 g) was treated with PPA (from 75 g P_2O_5 and 45 ml syrupy phosphoric acid) at 97°

for 1/2 hr. The usual work up furnished the above tetralone XX (with the elimination of isopropyl group) which was purified by distillation, b.p. 126-28°/1 mm, yield 10.218 g (39.86%). The ketone solidified immediately and crystallised from pet. ether m.p. 59-60° (Lit.[39]: b.p. 163-4°/12 mm) (Found: C, 82.7; H, 8.37. $C_{13}H_{16}O$ requires: C, 82.93; H, 8.57%). $\lambda_{max}^{ethanol}$ 328, 253 mμ. ε, 1914, 10480. IR: $\nu^{C=O}$ 1678 cm^{-1}.

Nitric acid oxidation of the above tetralone (XX; 0.2 g) followed by esterification of the resulting acid (0.19 g) with diazomethane furnished the tetramethyl ester of mellophanic acid (XXIb) which was crystallised from methanol m.p. 106-107° (Lit.[40]: m.p. 107-09°), yield 0.150 g.

(ii) $AlCl_3$ method: PCl_5 (0.3720 g) was placed in a distillation flask (100 ml, side tube plugged) and covered with dry benzene (15 ml). The acid (1 g) dissolved in dry benzene (5 ml) was added in two lots to PCl_5. Benzene and $POCl_3$ were removed by distillation under vacuum at < 90°. Anhydrous $AlCl_3$ (0.689 g, 1.1 mol) was placed in a conical flask carrying a guard tube and immediately covered with dry benzene (thiophene free) and chilled to -10°. The acid chloride thus prepared was taken up in thiophene-free benzene chilled to ~5° and was added all at once to $AlCl_3$-benzene mixture and swirled. On warming to room-temperature the reaction started with the evolution of HCl gas. After the vigour of the reaction had subsided the reaction product

was warmed to 50° till all the $AlCl_3$ dissolved. The reaction mixture was then poured onto ice (20 g) and HCl (conc. 2 ml), and kept for 1/2 hr with occasional stirring. Ether (25 ml) was added and the red solvent layer removed, washed with dil HCl (10 ml x 2), water (20 ml x 2), aq. NaOH (5%, 10 ml x 2), water (10 ml x 3) and dried. The solvent was removed and the residue distilled, b.p. 122-3°/0.8 mm, m.p. 57.5-59.5°, yield 0.586 g (77.31%). Mixed m.p. with PPA cyclised product (m.p. 59-60°) remained undepressed proving the elimination of isopropyl group during this cyclisation also.

1,3,6-Trimethylnaphthalene (XXII)

The tetralone (XX; 2.0 g, 1 mol) in ether (20 ml) was reduced with $LiAlH_4$ (0.404 g, 1 mol) in dry ether (60 ml) and the carbinol (1.8962 g, 92.32%) was heated with iodine (50 mg) to furnish the dialin which was distilled over Na, b.p. 115-17°/2 mm, n_D^{30} 1.5646, yield 1.4520 g (85%). (Found: C, 90.80; H, 9.085. $C_{13}H_{16}$ requires: C, 90.64; H, 9.36%). $\lambda_{max}^{ethanol}$ 268, 225, 219-225 mμ. ε, 15480, 51170, 48150 resp.

The above dialin (1.429 g) and sulphur (0.2178 g) were heated together at 210-20°/200 mm for 3 hr. The product was distilled over a pinch of Cu. powder, b.p. 126-29°/0.9 mm, n_D^{29} 1.5874, yield 1.337 (95.2%).

The trinitrobenzene complex was prepared in the usual manner, m.p. 147-49°. From different experiments a total quantity of 4.8126 g of the TNB complex was collected.

An analytical sample had m.p. 148-50° (Found: C, 59.7; H, 4.2; N, 11.1. $C_{19}H_{17}O_6N_3$ requires: C, 59.53; H, 4.47; N, 10.96%).

Pure sample of 1,3,6-Trimethylnaphthalene: The above TNB complex (m.p. 147-49°, 4.356 g) was passed through a column of basic Al_2O_3/I (160 g, 22cm x 3 cm) using pet. ether for elution. On solvent removal the regenerated hydrocarbon was distilled over Na, b.p. 119-20°/1.5 mm, n_D^{30} 1.5976; d_4^{30} 0.9800; M_D 58.19, EM_D 2.6310, $E\Sigma_D$ 1.5830. (Lit.[24,41,42]: b.p. 140-44°/10 mm; 115-20°/3 mm; 104-106°/1 mm resp.).

2,5,7-Trimethyl-8-isopropyltetralone-1 (XXIII):

PCl_5 (9.2 g) was placed in a 500 ml R.B. flask with a $CaCl_2$ guard tube and was covered with thiophene-free benzene (60 ml) to which the acid (10.0 g) was added and the whole mixture was swirled well till all the PCl_5 dissolved. The acid chloride thus prepared following the method already described in detail, was chilled to ~-5° and to it anhydrous $SnCl_4$ (10 ml) in benzene (thiophene-free) (10 ml) was added in one lot and the whole mixture was swirled very vigorously for 5 minutes. The reaction mixture which was deep red in colour was left as such for 1/2 hr when the colour changed to dirty brown. The reaction product was then treated with crushed ice (250 g), conc. HCl (80 ml) and ether (50 ml). The ether layer was removed and the aqueous part extracted with ether (50 ml x 5). The combined extracts were washed with

dil HCl (5%,80 ml x 4), water (100 ml x 2), aq. NaOH (5%,80 ml x 4), water (100 ml x 3) and dried. The solvent was flashed off and the residue distilled to give the required tetralone, b.p. 145-47°/3 mm, n_D^{28} 1.5442, yield 8.766 (32.54%). (Found: C, 83.4; H, 10.0. $C_{16}H_{20}O$ requires: C, 83.43; H, 9.6%). $\lambda_{max}^{ethanol}$ 303 mμ, ε 2050; 257 mμ, ε, 8213; 220 mμ, ε, 24090. IR: $\nu^{C=O}$ 1683 cm^{-1} and 1678 cm^{-1}.

Nitric acid oxidation of the above tetralone (XXIII; 0.22 g) followed by the esterification by diazomethane of the acid (0.24 g) furnished an ester which crystallised from methanol (0.19 g) m.p. 148-50°, identical with that of pentamethyl ester of 1,2,3,4,5 benzene pentacarboxylic acid XXIV (Lit.[36]: m.p. 149-50°). Mixed m.p. with pyromellitic acid ester (VIb) (140-42°) was depressed (115-30°).

1,3,6-Trimethyl-4-isopropyl-7,8-dihydronaphthalene (XXVI)

The tetralone (XXIII; 3.0 g, 1 mol) in ether (30 ml) was reduced with a slurry of $LiAlH_4$ (0.539 g, 1.1 mol) in dry ether (100 ml) at ~ -5° and the usual work up gave the carbinol (XXV; 2.859 g, 94.48%) which was dehydrated by heating it with iodine (0.100 g). The dialin thus obtained was distilled over Na, b.p. 136-37°/2 mm, n_D^{28} 1.5602, yield 2.5696 g (97.18%) (Found: C, 89.9; H, 10.2. $C_{16}H_{22}$ requires: C, 89.65; H, 10.35%). $\lambda_{max}^{ethanol}$ 263, 223.5 – 225 mμ. ε, 15150, 50190 resp.

3-Methylcadalene (XXVII)

The dialin (XXVI; 2.538 g) was dehydrogenated with

sulphur (0.330 g) at 205-10°/200 mm for 3 hr. 3-Methylcadalene was directly distilled off over a pinch of Cu. powder, b.p. 132-34°/2.5 mm, $n_D^{28.5}$ 1.5834; yield 2.3840, 94.82%.

Trinitrobenzene derivative: The trinitrobenzene complex was prepared from 2.384 g of the above hydrocarbon in the usual way, m.p. 160-62°. Total quantity of the TNB adduct collected by different experiments amounted to 6.645 g. An analytical sample had the m.p. 162-63° (Lit.[2]: 165°) (Found: C, 61.9; H, 5.6; N, 10.1. $C_{22}H_{23}O_6N_3$ requires: C, 62.16; H, 5.45; N, 9.88%).

Pure sample of 3-methylcadalene: The TNB complex of 3-methylcadalene (5.490 g, m.p. 162-63°) was passed through a column of basic Al_2O_3/I (200 g, 25 cm x 3.5 cm) using pet. ether as the eluent. The regenerated hydrocarbon was finally distilled over Na, b.p. 120-21°/1.5 mm, (Lit.[2]: b.p. 145°/4 mm), n_D^{30} 1.5240, M_D 72.97 RM_D 3.6170 $R\Sigma_D$ 1.7060.

Trinitrotoluene compound: The trinitrotoluene complex was prepared from the pure sample of 3-methylcadalene (0.200 g) in the manner already described. It had m.p. 97-98.5° (Found: C, 63.22; H, 5.38. $C_{23}H_{25}O_6N_3$ requires: C, 62.86; H, 5.93%).

5-METHYLCADALENE

β-(p-Cymoyl-2-) α-methylpropionic acid (XXVIII)

Methylsuccinic anhydride (28 g, 1 mol) was condensed

with p-Cymene (III; purified by H_2SO_4 method, 41 ml ≡ 35 g, 1.1 mol) by Friedel-Crafts method using nitrobenzene (150 ml) and anhydrous aluminium chloride (74 g, 2.2 mol) following the procedure already described. Yield of the crude keto acid was 76.8%. It crystallised from benzene-pet. ether mixture (1:2), m.p. 118-19°, yield 24 g, 60.25% (Lit.[2]: m.p. 118-19°, yield of the crude acid 80.5%, yield of the pure product 60%).

γ-(p-Cymyl-2-)α-methyl butyric acid (XXIX)

The above keto acid (26 g) was reduced to the required acid (XXIX) by Clemmensen's method using Zn-amalgum (Zn-amalgum; Zn wool 64 g, $HgCl_2$ 6.4 g, HCl con. 4 ml and H_2O, 95 ml) and HCl (112 ml conc + 47 ml H_2O) with the addition of toluene (64 ml) and gl. acetic acid (3.5 ml) and by refluxing for 34 hr at 120-40°. Usual work up furnished the required product, b.p. 158-60°/1 mm, yield 20.488 g (83.5%). (Lit[2]: b.p. 176-78°/3 mm, yield 80-95%).

2,5-Dimethyl-8-isopropyl tetralone-1 (XXX)

(1) By $AlCl_3$ method: The acid chloride [prepared from the acid (XXIX) 10 g and PCl_5 16 g] was treated with anhydrous $AlCl_3$ in n-heptane as described early, and the usual work up gave the required tetralone (XXX) as a colourless liquid, b.p. 132-34°/1.5 mm, yield 13.228 (96%) (Lit[2]: b.p. 141-42°/3 mm, yield 87%). The tetralone solidified after a day, m.p. 50-51°. $\lambda_{max}^{ethanol}$ 302, 253, 217 mμ, ε, 2134, 9475, 21440 resp. Ir: $\nu^{C=O}$ 1681 cm^{-1}.

(ii) By PPA method: The above acid (XXIX; 4 g) was treated with PPA (20.g P_2O_5 and 12 ml syrupy phosphoric acid) at 97° for 1/2 hr with occasional stirring and then worked up in the usual manner to give the required tetralone, b.p. 120°/1 mm, n_D^{30} 1.5551, yield 2.333 g (63.31%). The above tetralone solidified after a day and crystallised from pet. ether, m.p. 50-1°. Mixed m.p. with the tetralone obtained by $AlCl_3$ method remained undepressed.

1,5,6-Trimethyl-4-isopropyl-7,8-dihydronaphthalene (XXXII)

(i) Methyl-lithium reaction: In a 3-necked flask carrying a dropping funnel, a stirrer and a condenser, Lithium (1.7 g 0.4A) was covered with dry ether (90 ml) and the apparatus was flushed with dry nitrogen and the contents were cooled in an ice-salt bath to -10°. Methyliodide (freshly distilled, 16.8 g,0.5 mol) in dry ether (35 ml) was added dropwise with stirring. When all the Lithium metal had dissolved (1/2 hr), the above tetralone XXX (3.336 g) dissolved in dry ether (15 ml) was added to the cold methyl-lithium solution dropwise and with stirring (1/2 hour). The reaction mixture was refluxed for 15 hr under nitrogen atmosphere. The product was chilled and cautiously treated with aq. NH_4Cl (20%, 30 ml); the solvent layer was separated and the aqueous part extracted with ether (50 ml x 3). The combined extracts were washed successively with water, aq. sodium thiosulphate (10%, 30 ml), water and dried. The solvent was flashed off when the crude carbinol XXXI weighed 3.2610 g (yield 91%) which was used as such in the

next step.

(ii) Dehydration: The above carbinol (3.261 g) and iodine (0.100 g) were heated together for 1 hr at 98-100° on a waterbath. The usual work up furnished the dihydronaphthalene (XXXII) which was distilled over sodium, b.p. 117-19°/1.5 mm (Lit.[2]: b.p. 140-43°/2.5 mm). $n_D^{28.3}$ 1.5475, yield 2.950 g.(98%).(Found: C, 89.16%; H, 10.5. $C_{16}H_{22}$ requires: C, 89.65; H, 10.35%). $\lambda_{max}^{ethanol}$ 262, 224.5, 219 mμ. ε, 9707, 20180, 23630 resp.

5-Methylcadalene (II)

The above dialin (1.7110 g) was dehydrogenated with sulphur at 205-210° for 3 hr under a slight suction. The product was directly distilled off in vacuum over freshly precipitated Cu powder, b.p. 122-28°/1.3 mm, n_D^{28} 1.5863, yield, 1.5000(88.5%). The TNB complex prepared in the usual manner was recrystallised from 80% acetic acid as orange needles, m.p. 110-11°, yield 2.020 g. The above experiments were repeated to collect a total of 5.802 g of the TNB complex with m.p. 109-11°. An analytical sample of the TNB complex had m.p. 112-13.5° (Lit.[2]: m.p. 160-61°) (Found: C, 62.4; H, 5.5; N, 10.1. $C_{22}H_{23}O_6N_3$ requires: C, 62.16; H, 5.45; N, 9.88%).

Pure sample of 5-Methylcadalene: The trinitrobenzene derivative (5.2700) was passed through a column of basic Al_2O_3/I (120 g, 25 cm x 3 cm) and eluted with pet. ether when pure

5-methylcadalene (2.5235 g) was obtained, b.p. 144-45°/1.5 mm, n_D^{30} 1.5906, d_4^{30} 0.9847, M_D 72.86, EM_D 3.5070 $E\Sigma_D$ 1.6550 (Lit.[2]: b.p. 132/1.5 mm).

Trinitrotoluene complex: The trinitrotoluene complex was prepared from the pure sample of 5-methylcadalene (0.200) and the TNT reagent (0.200) in the usual way. The derivative was crystallised twice from ethanol, m.p. 86-87.5° (Lit.[2]: 87-88°) (Found: C, 62.4; H, 5.5. $C_{23}H_{25}O_6N_3$ requires: C, 62.86; H, 5.73%).

7-METHYLCADALENE

β-(p-Cymoyl-2)-α:α-dimethylpropionic acid (XXXIII)

Dimethyl succinic anhydride (10 g, 1 mol) was condensed with p-cymene (III; purified by H_2SO_4 method, 21.52 g, 1.1 mol) by Friedel-Crafts method using nitrobenzene (50 ml) and anhydrous aluminium chloride (28 g, 3 mol), by following the procedure already detailed. The usual work up gave the required acid, yield 9.8 g.(50.12%). As the keto acid was gummy in nature its purification was done via its methyl ester as detailed below.

The crude acid (XXXIII; 9.8 g) was mixed with benzene (10 ml), anhydrous methanol (10 ml) and conc. H_2SO_4 (1 ml) and refluxed for 10 hr. Working up of the product in the usual manner gave the required ester, b.p. 134-39°/1 mm yield 5.6 g (56.71%) (Lit.[43]: b.p. 148-9°/2 mm).

The above keto ester (9.8 g) was hydrolysed by

refluxing with alcoholic KOH (10%,65 ml) for 15 hr. The acid obtained after an usual work up was a brown gummy product, yield 8.7 g.

2-(p-Cymyl-2-)-3,3-dimethyl butyric acid (XXXIV)

The keto acid (XXXIII; 8.7 g) was reduced with Zn-amalgam (from 30 g Zn-wool, 2 g $HgCl_2$, 2 ml conc. HCl, 20 ml H_2O) and dil HCl (conc. HCl 32 ml, 13 ml H_2O) and toluene (21 ml) by refluxing for 48 hr. The product was worked up as detailed earlier and the required acid was purified by distillation, b.p. 150-53°/0.8 mm, yield 5.8 g (70.44%).

2,3,5-Trimethyl-8-isopropyl-tetralone-1 (XXXV)

To PPA (from 25 g P_2O_5 and 15 ml syrupy H_3PO_4) maintained at 95°, the above acid (4.7 g) was added and the whole mixture was maintained at 97° for 1/2 hr with occasional stirring. The product was worked up in the same manner as described early and the tetralone was purified by fractionation, b.p. 125-27°/0.8 mm, yield 3.6 g(81.93%). $\lambda_{max}^{ethanol}$ 300 mμ, 251.6, 217 mμ ε, 1643, 7645, 19770 resp. IR: $\nu^{C=O}$ 1681 cm^{-1} and 1783 cm^{-1}.

1,6,7-Trimethyl-4-isopropyl, 7-8 dihydronaphthalene (XXXVII)

The tetralone (XXXV; 4 g, 1 mol) in ether (40 ml) was reduced with $LiAlH_4$ (0.660 g, 1 mol in 120 ml ether) in the usual manner and worked up to give the crude carbinol XXXVI (3.9425 g) (97.7%), which was mixed with iodine (0.100 g)

and heated for 1 hr at ~ 95°. On working up the product the dialin XXXVII obtained weighed, 3.5524 g (97.68%) of which 0.3479 g was distilled over Na, b.p. 117-19°/1 mm, $n_D^{28.5}$ 1.5425, yield 0.7878 g (Found: C, 89.17; H, 10.4. $C_{16}H_{22}$ requires: C, 89.65; H, 10.35%). $\lambda_{max}^{ethanol}$ 271, 225, 219 mμ. ε, 12350, 36920, 35180 resp.

7-Methylcadalene (XXXVIII)

The above dialin (3.206 g) was dehydrogenated with sulphur (0.550 g) at 210-15°/200 mm for 3 hr. The product was distilled over a pinch offreshly prepared copper, b.p. 128-30°/1 mm, n_D^{29} 1.5782, yield 2.6125 g.(82.19%).

TNB derivative: The TNB complex was prepared (from 2.6125 g of the hydrocarbon) in the usual manner, m.p. 122-24°, yield 4.022 g. An analytical sample had the m.p. 126-27° (Found: C, 62.61; H, 5.4; N, 9.64. $C_{22}H_{23}O_6N_3$ requires: C, 62.16; H, 5.45; N, 9.88%).

Pure sample of 7-methylcadalene: The TNB complex (2.80 g) was passed through a column of basic Al_2O_3/I (80 g, 18 cm x 2.5 cm) using pet. ether as the eluent and the regenerated hydrocarbon was distilled over Na, b.p. 139-40°/1.5 mm, yield 1.3236 g. The hydrocarbon solidified on standing. m.p. 39-40° (Lit.[1]: b.p. 135-37°/2.5 mm, m.p. 39.5-40°).

TNT derivative: From 0.200 g of the above pure hydrocarbon TNT complex was prepared, and crystallised twice from ethanol. m.p. 72-73° (Found: C, 62.84; H, 5.7. $C_{23}H_{25}O_6N_3$ requires:

C, 62.86; H, 5.73%).

8-METHYLCADALENE

4-(p-Cymoyl-2-)α-methylpropionic acid (XXVIII)

Methylsuccinic anhydride (48 g, 1 mol) was condensed with p-cymene (71 ml, 1.1 mol) using nitrobenzene and anhydrous $AlCl_3$ (130 g, 2.2 mol) by the method already described. The required acid obtained had the m.p. 118-19°, yield 45.5 g,(39.65%).

Methyl-4-(p-cymoyl-2-)α-methylpropionate (XXVIIb)

The above acid (45.5 g) was mixed with benzene (90 ml), anhydrous methanol (90 ml) and conc. H_2SO_4 (8 ml) and refluxed for 12 hr. Usual work up furnished the required product: b.p. 152-54°/1.5 mm, yield 43.680 g (90.88%) (Lit.[44]: b.p. 145°/0.5 mm, yield 75%).

4-(p-Cymyl-2-)α-γ-dimethylvinylacetic acid (XXIX)

Inverse Grignard reaction:

In a three-necked flask carrying a dropping funnel, a stirrer and a condenser, the above keto ester (11 g) was taken in dry ether (70 ml) and chilled in an ice-salt bath. The apparatus was flushed with nitrogen and the Grignard solution of methyl magnesium iodide [prepared from magnesium (1.35 g,1.7M), methyliodide (7.7 g, 1.7M) and dry ether (35 ml) in the usual manner under nitrogen atmosphere] was transferred to the dropping funnel under nitrogen atmosphere and

was added dropwise to the chilled ester with stirring (1/2 hr). The reaction mixture was allowed to stand as such for two hr when it attained room temperature and then it was refluxed on a waterbath for 3 hr and finally left as such overnight (12 hr). The reaction product was chilled and cautiously treated with dil HCl (1:1) (60 ml). The reddish ether layer was separated and the aq. part extracted with ether (50 ml x 4). The combined extracts were washed with water and then extracted with aq. Na_2CO_3 (5%,25 ml x 4). The alkaline extract was treated with Norite, chilled and acidified with dil HCl (congo red) and the liberated oil was extracted with ether (25 ml x 4). The combined ether extracts were washed with water and dried. On removing the solvent the residual viscous liquid weighed 1.480 g, 14.33%.

Neutral part: The ether extract after removing the acidic part was washed with water and dried. The residue (9.8 g) obtained after the solvent removal was hydrolysed with KOH (alcoholic, 10%, 50 ml) by refluxing on a waterbath for 6 hr. The alcohol was distilled off, the product diluted with water and extracted with ether to remove any unhydrolysed neutral fraction (1.4 g). The alkaline solution was boiled with norite, cooled and acidified with HCl (congo red). The liberated oil (8.20 g) was separated and digested with dil HCl (1:1 10 ml) on a waterbath for 2 hours.

This treatment converted the unsaturated acid into lactone (XL) whereas the keto acid (XXVIII) remained unaffected. The product was then taken up in ether, separated into acid (XXVIII) and neutral fractions (XL). The neutral fraction which consisted of the lactone (XL) weighed 4.0 g (38.74%) and the acid (XXVIII) weighed 3.0 g. Total yield of the acid-lactone mixture was 53%.

The experiments were repeated to collect more of the acid XXIX (6.360 g) and the lactone XL (17.670 g).

γ-(p-Cymyl-2-)-α-γ-dimethylbutyric acid (XLI)

The above lactone-acid mixture (8.4 g), red phosphorous (5.3 g), hydriodic acid (45 g) were refluxed at 130-40° for 60 hr. The reaction mixture was cooled, diluted with water, extracted with ether (60 ml x 5) and separated into acidic and neutral portions. The usual work up furnished the required acid XLI 7.163 g (84.53% crude) and the tetralone XLII (1.010, 12.96% crude). Another experiment with the above quantities mentioned with refluxing for 12 hr yielded the acid (XLI) 6.045 g (71.37% crude) and the tetralone XLII 1.285 g (16.36%). The acid (XLI; 15.2 g) was further purified by distillation. b.p. 156-68°/1 mm, yield 11.758 g (Lit.[44]: b.p. 145-55°/0.5 mm).

2,4,5-Trimethyl-8-isopropyltetralone-1 (XLII)

To PPA (from 42 g P_2O_5 and 26 ml syrupy phosphoric acid) maintained at 97°C the acid (XLI) 8.5 g, was added all at once

with stirring. Heating was continued for 1/2 hr but with occasional stirring. The reaction product was worked up in the usual manner and the tetraloneXLII was obtained as a colourless liquid, b.p. 117-18°/1 mm (lit.[94]: b.p. 115-17°/1 mm), yield 7.2215 g (91.62%). The ketone solidified on standing and crystallised from pet. ether, m.p. 43-44° (Found: C, 83.43; H, 9.51. $C_{16}H_{22}O$ requires: C, 83.47; H, 9.56%). $\lambda_{max}^{ethanol}$ 301, 254 and 218.5 mμ. ε, 2448, 9055 and 21000 resp.

2,4,5-Trimethyl-8-isopropyl-7,8-dihydronaphthalene (XLIV):

The above tetralone (XLII; 2 g 1 mol) in ether (20 ml) was reduced with $LiAlH_4$ (.330 g, 1 mol, ether 60 ml) in the usual manner and worked up to give the crude carbinol XLIII (1.988 g; 98.60%) which was heated with iodine (0.100 g) for 1 hr at 98-100° on a waterbath. The usual work up furnished the required dialinXLIV which was purified by distillation over Na, b.p. 112-14°/2.5 mm, n_D^{29} 1.5431, yield 1.5051 g (82.02%) (Found: C, 89.35; H, 10.26. $C_{16}H_{22}$ requires: C, 89.65; H, 10.35%). $\lambda_{max}^{ethanol}$ 271, 233, 225.5, 218 mμ. ε, 12630, 25280, 36110, 31780 resp.

8-Methylcadalene XLV

A mixture of the above dialin (1.5051 g) and sulphur (0.260 g) were heated together at 205-10° for 3 hr under slight suction. The product was distilled off over a pinch of copper powder, b.p. 120-22°/1.2 mm. n_D^{29} 1.5714,

yield 1.0482 g,(70.3%).

Trinitrobenzene derivative: The TNB adduct of 8-methylcadalene was prepared in the usual manner (TNB reagent 1.0482 g, 8-methylcadalene 1.0482 g) and was crystallised from 90% acetic acid, m.p. 116-17°, yield 0.9 g. An analytical sample had m.p. 116-17° (Lit.[2,31]: m.p. 118-18.5°, 117.5° resp.) (Found: C, 62.2; H, 5.4; N, 9.94. $C_{22}H_{23}O_6N_3$ requires: C, 62.16; H, 5.45; N, 9.88%). From several experiments the TNB complex of 8-methylcadalene (m.p. 116-17°) obtained amounted to 3.4838 g.

Pure sample of 8-Methylcadalene: The above TNB derivative (2.9560 g, m.p. 116-17°) was passed through a column of basic Al_2O_3/I (100 g, 22 cms x 2.5 cms) and eluted with pet. ether when pure 8-methylcadalene was obtained, b.p. 135-36°/1.5 mm, n_D^{30} 1.5876, d_4^{30} 0.9800, M_D 72.74, EM_D 3.3870, $E\Sigma_D$ 1.5380 (Lit.[2,31]: b.p. 144-47°/3 mm; b.p. 101-104°/0.15 mm, n_D^{20} 1.5911, m.p. 21.5°).

Trinitrotoluene complex: The TNT complex was prepared in the usual manner (from pure 8-methylcadalene 0.200 g and TNT reagent 0.200 g) but it was found to be unstable. m.p. 46-64° (Lit.[31]: m.p. 56-61°).

1,2,7-TRIMETHYL-4-ISOPROPYLNAPHTHALENE

α-methyl-γ-(3,4-dimethyl-6-isopropylphenyl)-butyric acid (XLVI)

The keto acid (V; 10 g) was reduced with Zn-amalgam (from 24 g Zn-wool, 2.4 g $HgCl_2$, 50 ml H_2O and 4 ml HCl conc) and HCl (70 ml conc. HCl and 24 ml H_2O) with the addition of

toluene (40 ml) and glacial acetic acid (4 ml) by the refluxing the whole mixture at 130-40° for 36 hr. The reaction product was worked up in the usual manner and the required acid XLVII was obtained as a thick colourless liquid, b.p. 160-70°/1 mm, n_D^{27} 1.5080, yield 8.8565 g (93.54%). (Found: C, 77.6; H, 9.8. $C_{16}H_{24}O_2$ requires: C, 77.39; H, 9.74%).

2,3,8-Trimethyl-5-isopropyltetralone-1 (XLVII)

To PPA (15 g P_2O_5 and 9 ml syrupy phosphoric acid) maintained at 97° in a 3-necked flask) 3.0 g of the above acid was added with stirring in one lot. The above temperature was maintained for 1/2 hr with occasional stirring of the reaction product, which was then worked up as detailed early to give the required tetralone, b.p. 134-37°/0.8 mm, yield 2.2555 g (81%). The tetralone solidified immediately, m.p. 60-64°. An analytical sample had the m.p. 64-65°. (Found: C, 83.20; H, 9.65. $C_{16}H_{22}O$ requires: C, 83.43; H, 9.63%). $\lambda_{max}^{ethanol}$ 308, 256, 214.5 mμ. ε, 2420, 9774, 30430 resp. IR: $\nu^{C=O}$ 1657 cm^{-1}. From another experiment a total of 4.6382 g of the tetralone was collected.

1,2,7-Trimethyl-4-isopropyl 5,6-dihydronaphthalene (XLIX)

The above tetralone (4.5 g,1 mol in 60 ml ether) was reduced with a slurry of $LiAlH_4$ (0.8905 g, 1.1 mol) in dry ether (140 ml) at ~ -5° and the resulting crude carbinol (XLVIII; 4.358 g, 96.01%) was treated with iodine (0.100 g) at 95-100° for 1 hr. The usual work up furnished the

dialin XLIX which was purified by distillation over Na, b.p. 123-25°/1 mm, n_D^{27} 1.5695, yield 3.9584 g (38.47%) (Found: C, 89.45; H, 10.47. $C_{16}H_{22}$ requires: C, 89.65; H, 10.35%). λ_{max}^{EtOH} 269, 226, 211 mμ; ε, 12900, 34150, 33360 resp.

1,2,7-Trimethyl-4-isopropylnaphthalene (L)

The above dialin XLIX; 2.5055 g) was mixed with sulphur (0.3847 g) and heated at 205-10°/200 mm for 3 hr. The product was distilled over a pinch of freshly precipitated Cu. powder, b.p. 130°/1mm, yield 2.4450 g (93.74%). The hydrocarbon solidified immediately, m.p 57-59.5°

Trinitrobenzene complex was prepared (from 1.9490 g hydrocarbon in ethanol(5 ml) and TNB reagent 1.9490 g in minimum amount of alcohol) in the usual manner, m.p. 133-34.5°. An analytical sample had the m.p. 134-35.5° (Found: C, 62.47 H, 5.2; N, 10.1. $C_{22}H_{23}O_6N_3$ requires: C, 62.16; H, 5.45; N, 9.88%).

Pure sample of 1,2,7-Trimethyl-4-isopropylnaphthalene: The TNB complex (2.4390 g) was passed through a column of basic Al_2O_3/I (100 g, 21 cms x 2.5 cms) using pet. ether for elution. The regenerated hydrocarbon was distilled over Na, b.p. 139-40°/1.5 mm, m.p. 59-60°

Trinitrotoluene complex: The TNT complex, prepared from the pure regenerated hydrocarbon (0.200 g) and the TNT reagent (0.200 g), was crystallised from ethanol, m.p. 73-74° (Found: C, 62.82; H, 6.0. $C_{23}H_{25}O_6N_3$ requires: C, 62.86; H, 5.73%)

SUMMARY

In connection with a study directed towards the characterisation of methylcadalenes by modern spectroscopic methods, all the five, theoretically possible, cadalenes have been prepared. New simpler procedures have been developed for all these cadalenes except for 5-methylcadalene which was obtained by a known procedure.

REFERENCES

1 W.P. Campbell and M.D.Soffer, J. Am. Chem. Soc., 64, 417 (1942).

2 a) Sukh Dev and P.C.Guha, J. Ind. Chem. Soc., 25, 13 (1948).

b) Sukh Dev, Ibid., 25, 69 (1948).

3 M.D.Soffer, C. Steinhardt, G. Turner and M.E.Stebbins, J. Am. Chem. Soc., 66, 1520 (1944).

4 L.H. Briggs and R.I. Taylor, J. Chem. Soc., 1338 (1947).

5 Sukh Dev and P.C.Guha, J. Ind. Chem. Soc., 26, 263 (1949).

6 S.B. Ghatge, R.K. Razdan and S.C.Bhattacharyya, Perf. and Ess. Oil 47, 157 (1956).

7 O. Motl, V. Sykora, V. Herout and F. Sorm, Coll. Czech. Chem. Comm. 23, 1297 (1958).

8 M.D.Soffer, M.Brey and J. Fournier, J. Am. Chem. Soc., 81, 1678 (1959).

9 S.C.Bhattacharyya, K.K. Chakravarti and K.L.Murve, Chemistry and Industry, 1352 (1959).

10 C.C.Kartha, P.S.Kalsi, A.M. Khaligram, K.K.Chakravarti and S.C.Bhattacharyya, Tetrahedron 19, 241 (1963).

11 O. Motl, V.G. Bucharov, V. Herout and F. Sorm, Chem.and Ind. 1759 (1963).

12 R.A. Smolders, Canad. J. Chem. 42, 2836 (1964).

13 F.M. Couchman, A.R.Pinder and in part M.H. Bromham, Tetrahedron 20, 2047 (1964).

14 A.S.Rao, K.L. Murve, K.K.Chakravarti and S.C.Bhattacharyya, Tetrahedron 19, 233 (1963).

15 K.L. Murthy, Ph.D thesis, Bombay University (1959).p.1

16 W. Cocker, B.L.Cross and J. McCormick, J. Chem. Soc., 72 (1952).

17a W. Cocker, B.L.Cross, J.T.Edward, D.S.Jenkinson and J.McCormick, J. Chem. Soc., 2355 (1953).

b W. Cocker and D.S.Jenskinson, J. Chem. Soc. 2420 (1954).

18 R. Anschütz and H. Immendorff, Ber. 18, 657 (1885).

19 C. Friedel and J.M. Crafts, Compt. rend. 100, 692 (1885)

20 O. Jacobsen, Ber., 18, 338 (1885).

21 N.P. Buu-Hoi and P. Cagniant, Bull. Soc. Chim. Fr. 11, 349 (1944).

22 Ullmann, Annalen 291, 19 (1896).

23 K. Miescher and J.H. Billeter, Helv. Chim. Acta. 22, 605 (1939).

24 Ruch Dev, J. Ind. Chem. Soc., 25, 333 (1948).

25 B.A.Nagasampagi, R.C.Pandey, V.H.Pansare, J.R.Prahlad and Ruch Dev, Tetrahedron Letters 8, 411 (1964).

26 W.L. Mosby, J. Am. Chem. Soc., 74, 2564 (1952).

27 J.D. Hedden and H.C.Brown, J. Am. Chem. Soc., 75, 3744(1953)

28 J.W. Huffman, J. Org. Chem. 24, 1759 (1959).

29 E.J. Christol, R. Jacquier and M. Mousseron, Bull.Soc.Chim. France, 248 (1958).

30 W.M. Schubert and W.A.Sweeney, J. Am. Chem. Soc., 77, 4172 (1955).

31 W.T.G. Johnston, J.C.Smith and C.N. Staveley, Chem. and Ind. 607, 1954.

32 E. Lederer and M. Lederer, Chromatography, p.24, Elsevier Publishing Co., New York (1957).

33 H. Brockmann and H. Schodder, Ber., 74, 73 (1941).

34 W.G. Whittleston, J. Am. Chem. Soc., 59, 826 (1937).

35 A. Klages, Ber., 32, 2306 (1906).

36 W.F. Campbell and M.D.Soffer, J. Am. Chem. Soc., 64, 425 (1942).

37 H.J. Shine, J. Org. Chem., 24, 252 (1959).

38 D.V. Nightingale and B. Carton Jr., J. Am. Chem. Soc., 62, 280 (1940).

39 L. Ruzicka, L. Ehmann and L. Hörgeli, Helv. Chim. Acta, 16, 323 (1933).

40 L.I.Smith and K.D. Byrkit, J. Am. Chem. Soc., 55, 4505 (1933).

41 L. Ruzicka, L. Ehmann, H. Arni and Ed. Bernasconi, Helv. Chim. Acta., 15, 154 (1932).

42 R.C.Gupta and M.S. Muthana, J. Ind. Inst. of Science, 35A, 310 (1953).

43 Idem., Ibid., 35A, 269 (1953).

44 Idem., Ibid., 35A, 131 (1953).

CHAPTER III

CHARACTERISATION OF METHYLCADALENES

CHARACTERISATION OF METHYLCADALENES

The spectral properties of methylcadalenes, the syntheses of which have been described in the previous Chapter, have been studied with a view to find out data characteristic of each hydrocarbon. This study was aimed at collecting information which would help to identify these, even in a mixture. In this connection the gas-liquid-chromatography (GLC) and thin-layer chromatography (TLC) have also been studied.

Ultraviolet absorption

The ultraviolet absorption characteristics of the various methylcadalenes as well as those of cadalene are summarised in Table 1 and graphically represented in Fig.1. As was anticipated, there is no significant difference in the UV absorption of the various isomeric methylcadalenes and all show the expected bathochromic shift[1,2,3] (due to four alkyl groups the expected red shift being of the order of 10-15 mμ) with respect to naphthalene*.

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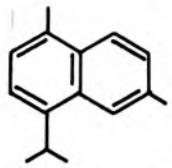
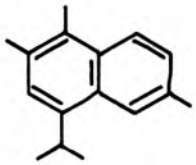
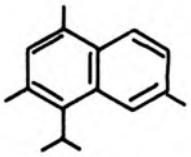
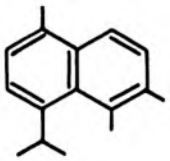
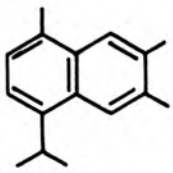
*Naphthalene has the following bands[3]:

λ_{max}	log ε
221 mμ	4.98
286 "	3.62
312 "	2.40

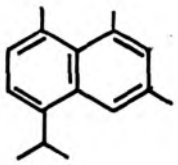
TABLE 1: ULTRAVIOLET ABSORPTION DATA OF METHYLCADALENES AND CADALENE.

No.	Compound	λ_{max} heptane (mμ)	ϵ_{max}
I	 ** CADALENE	326 297 (S)* 289 284 (S) 280 (S) 227	781 5403 6397 6042 5749 61490
II	 2-METHYLCADALENE	329 323 (S) 293 (S) 284 235	724 842.0 5843 6166 77180
III	 3-METHYLCADALENE	322 292 283(S) 232	4364 6306 6336 84160
IV	 5-METHYLCADALENE	331 297 289 (S) 235	655.7 7464 6664
V	 7-METHYLCADALENE	322 (S) 290 281 269 (S) 235 229-34	452 6145 5367 4341 73310 65800

Contd.....

S - Shoulder.

TABLE 1 (Contd.)

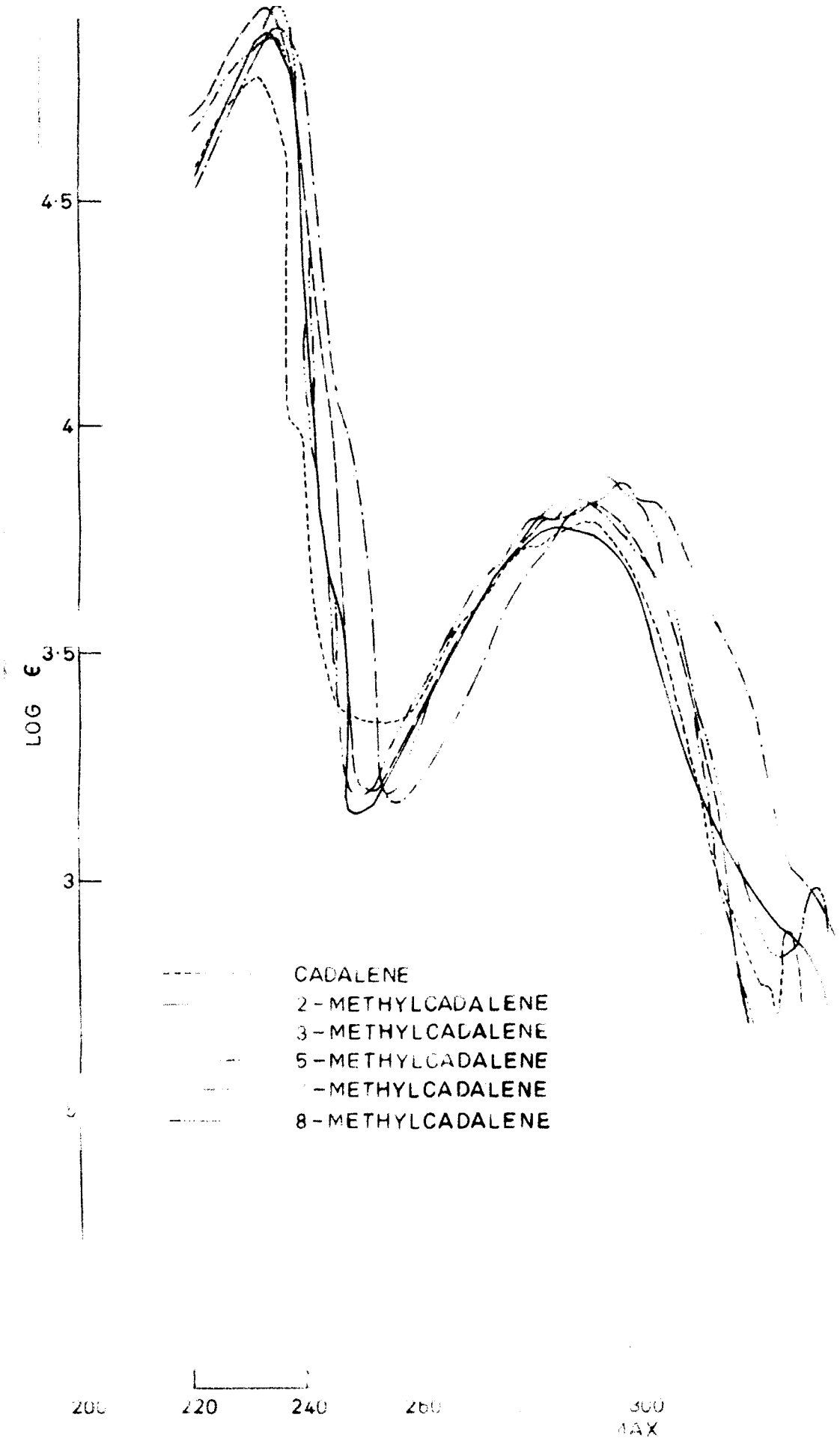
No.	Compound	$\lambda_{max}^{heptane}$ (mμ)	ϵ_{max}
VI		331 302 (S) 293 287 (S) 282 229-36 (S)	952.6 6409 7860 7194 6435
	8-METHYLCADALENE		

S* - Shoulder

** cf. R.A. Morton and A.J.A. Delouveia, J. Chem. Soc. 935 (1934).

L. Ruzicka, H. Schinz and P.H.Müller, Helv. Chim. Acta 27 (197) (1944).

R.P. Hildebrand and M.D.Sutherland, Aust. J. Chem. 12, 678 (1959).


4·5
4
3·5
3
LOG ε
CADALENE
2-METHYLCADALENE
3-METHYLCADALENE
5-METHYLCADALENE
-METHYLCADALENE
8-METHYLCADALENE
200
220
240
260
300
MAX

Infrared absorption

The infrared spectra of the various methylcadalenes and cadalene are shown in Figs.2 - 7. The differentiating features in the infrared spectra of isomeric aromatic compounds are the out-of-plane deformation of nuclear hydrogen observable in the regions 650-1000 cm^{-1} and the absorption patterns in the 1660-2000 cm^{-1} region.

650-1000 cm^{-1} region: The 650-1000 cm^{-1} region has been used extensively[4] in determining the substitution pattern in benzene derivatives. The applications of these correlations to variously substituted naphthalenes has been considered by Cencelz and Hädz[5] who concluded that the original benzene substitution rules are quite applicable in the case of naphthalenes, but the number of bands considerably exceeds those expected on the basis of these rules; and it was suggested that the absence of a particular band is more diagnostic than its presence. Work on these lines has also been reported by Whiffen et al.[6], Werner et al.[7], and Luther and Dunzler[8].

The methylcadalenes for the purpose of present discussion can be divided into a group consisting of 2-, 3-, 7-, and 8-methylcadalenes (two adjacent hydrogens and two lone hydrogen atoms) and 5-methylcadalene (two sets of two adjacent hydrogens) which are expected to display strong peaks in the 800-860 cm^{-1} and 860-900 cm^{-1} regions, and only in the 800-860 cm^{-1} region respectively; and as can be seen from the spectra this is borne out. Further

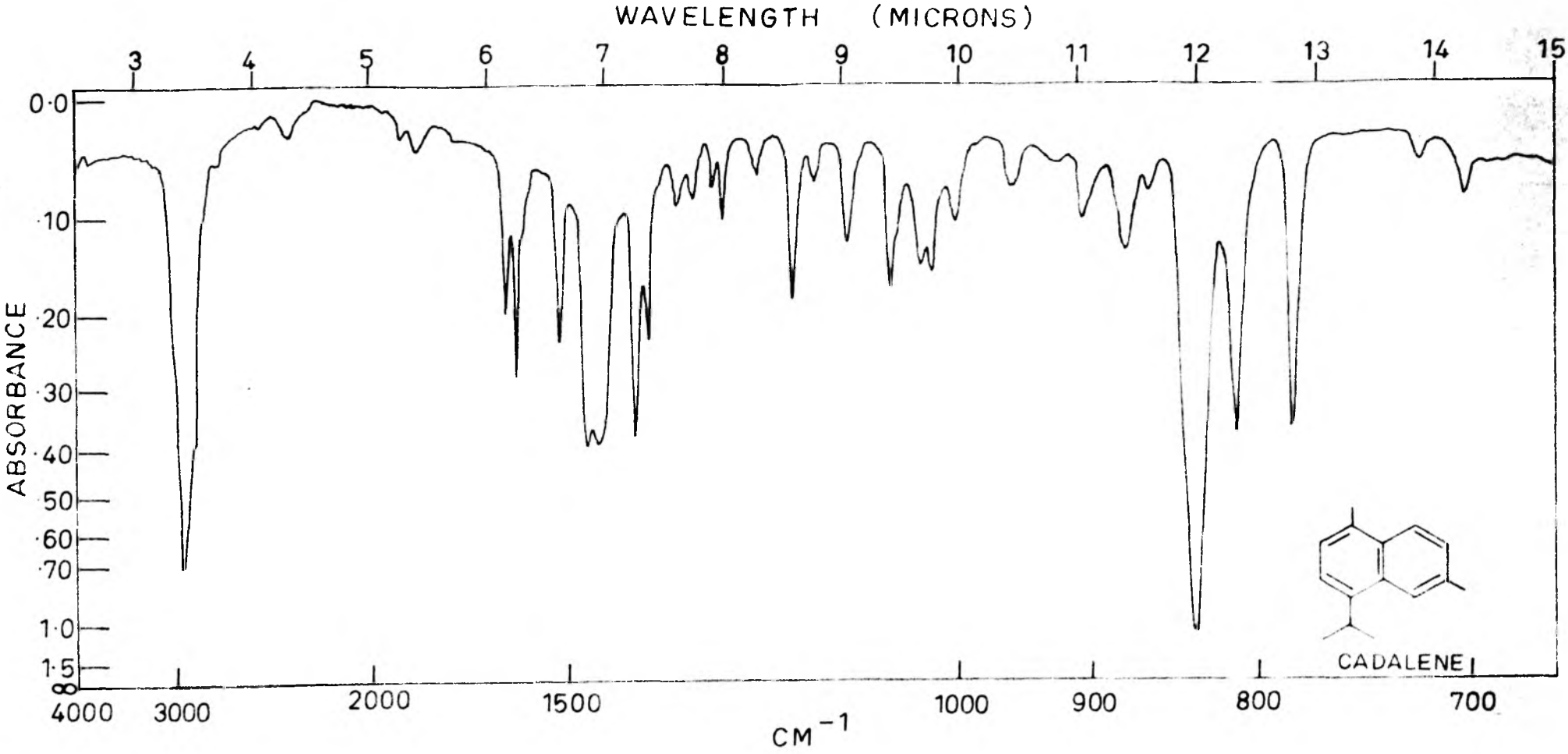


FIG. 2. IR SPECTRUM OF CADALENE

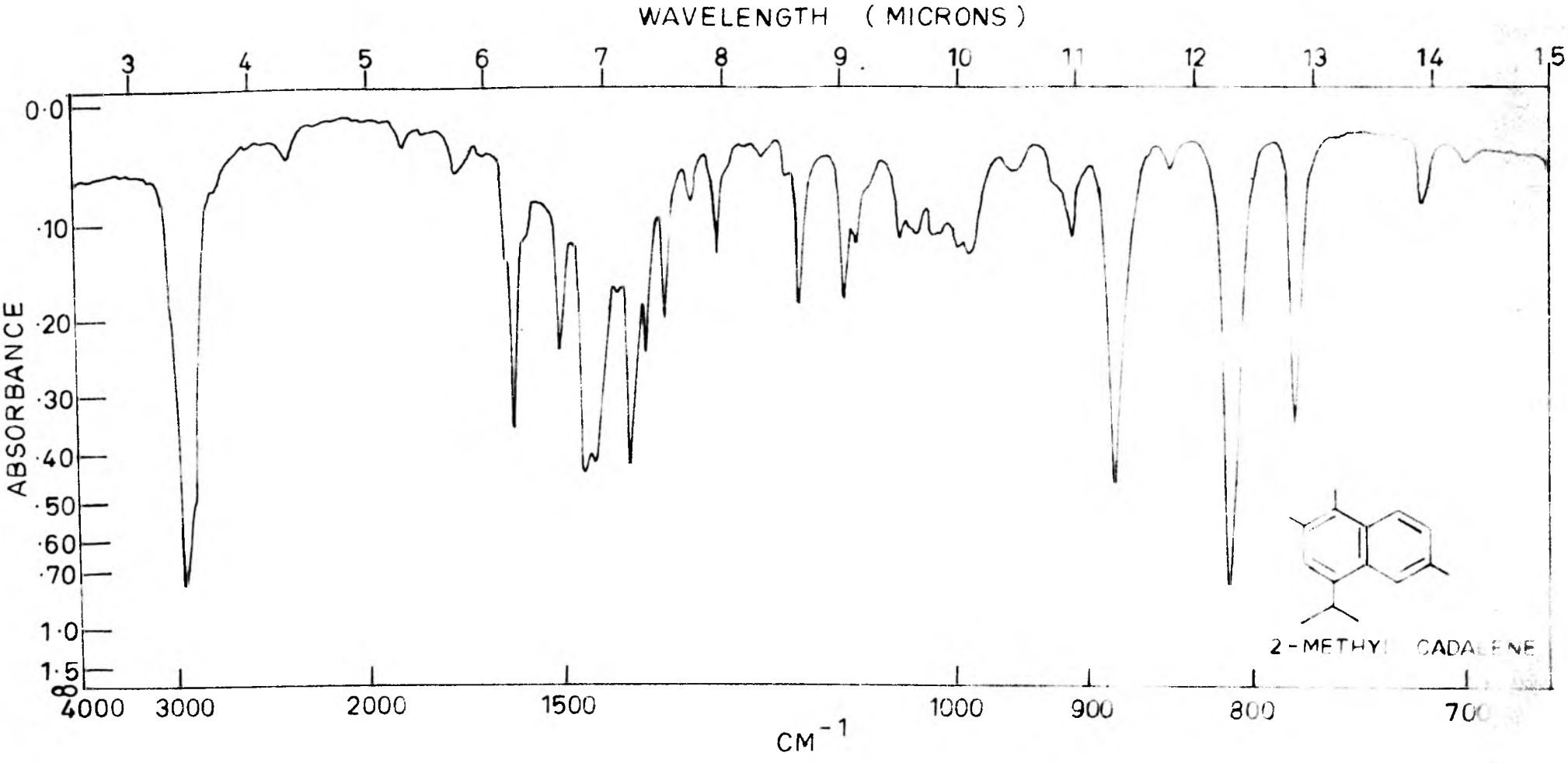


FIG. 3. IR SPECTRUM OF 2-METHYL CADALENE

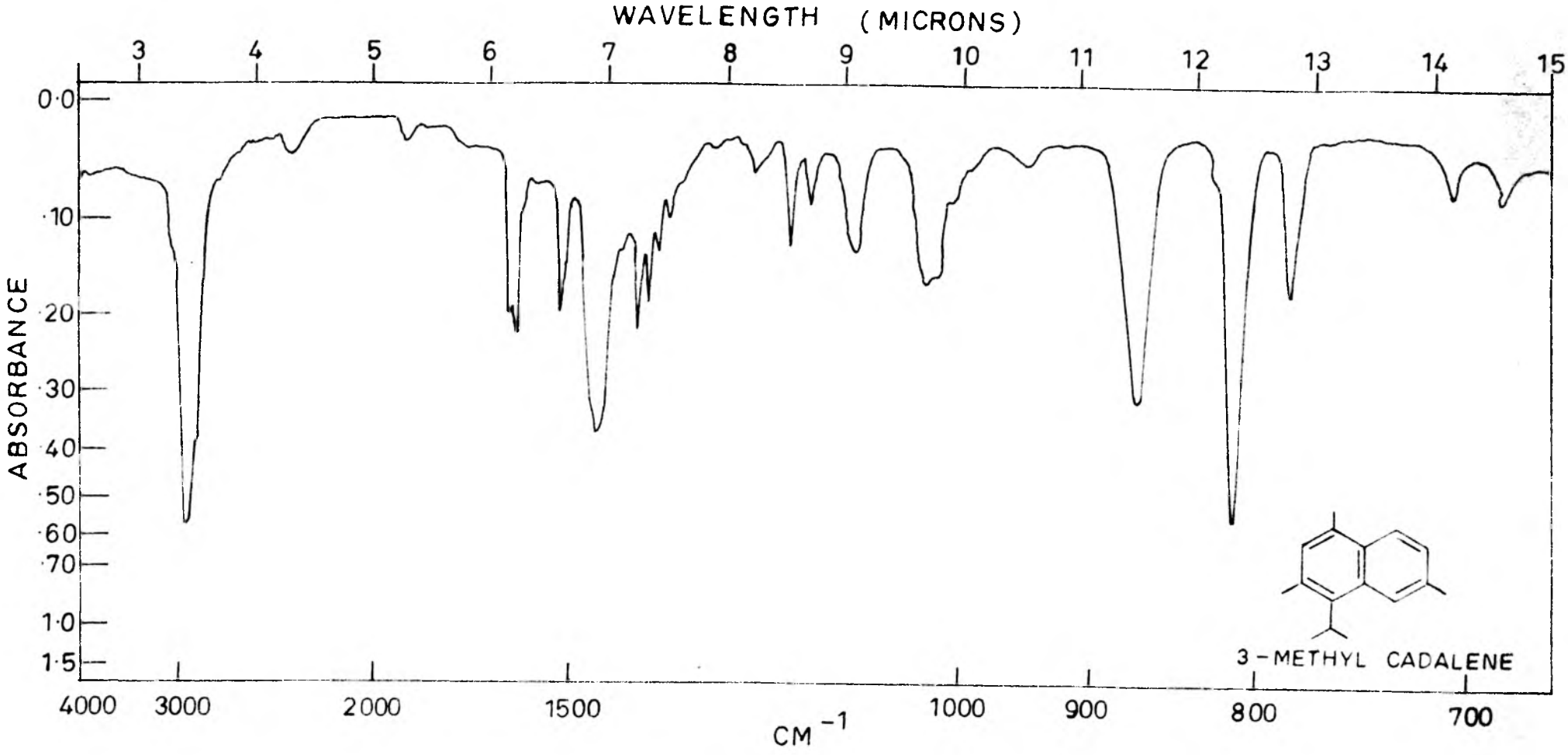
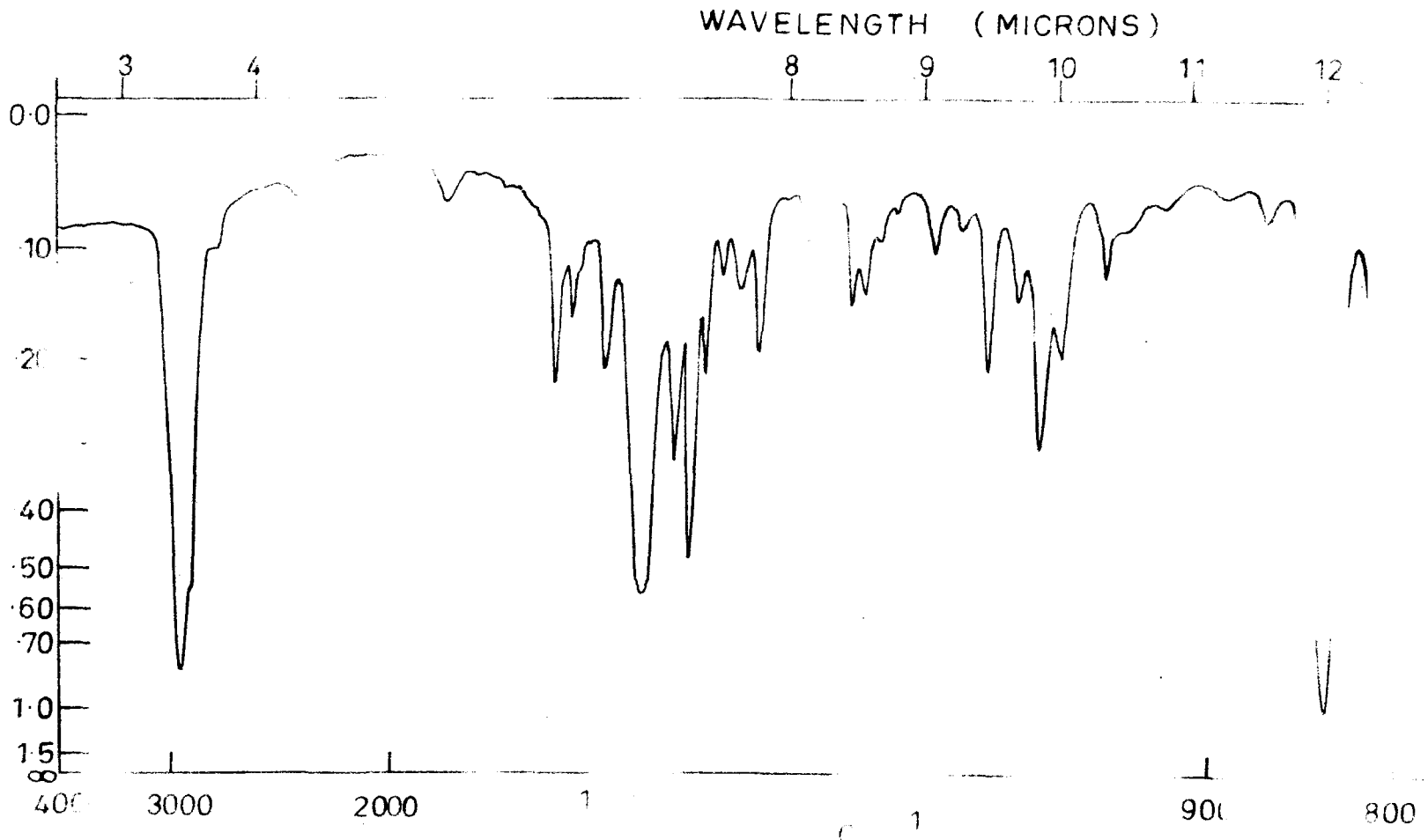


FIG. 4. IR SPECTRUM OF 3-METHYL CADALENE



5 [illegible] SPECTRUM OF 5-METHYL CADALENE

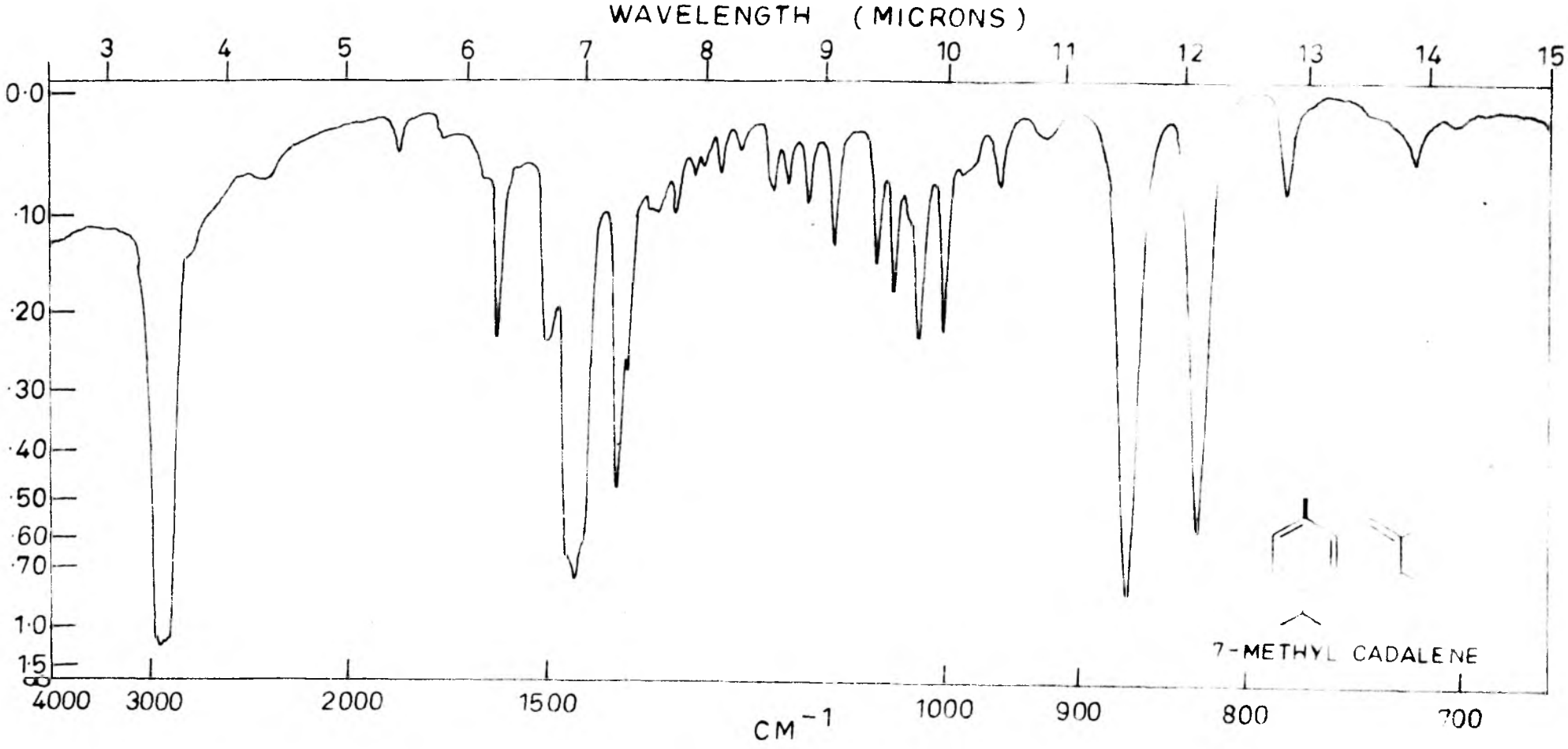


FIG. 6. IR SPECTRUM OF 7- METHYL CADALENE

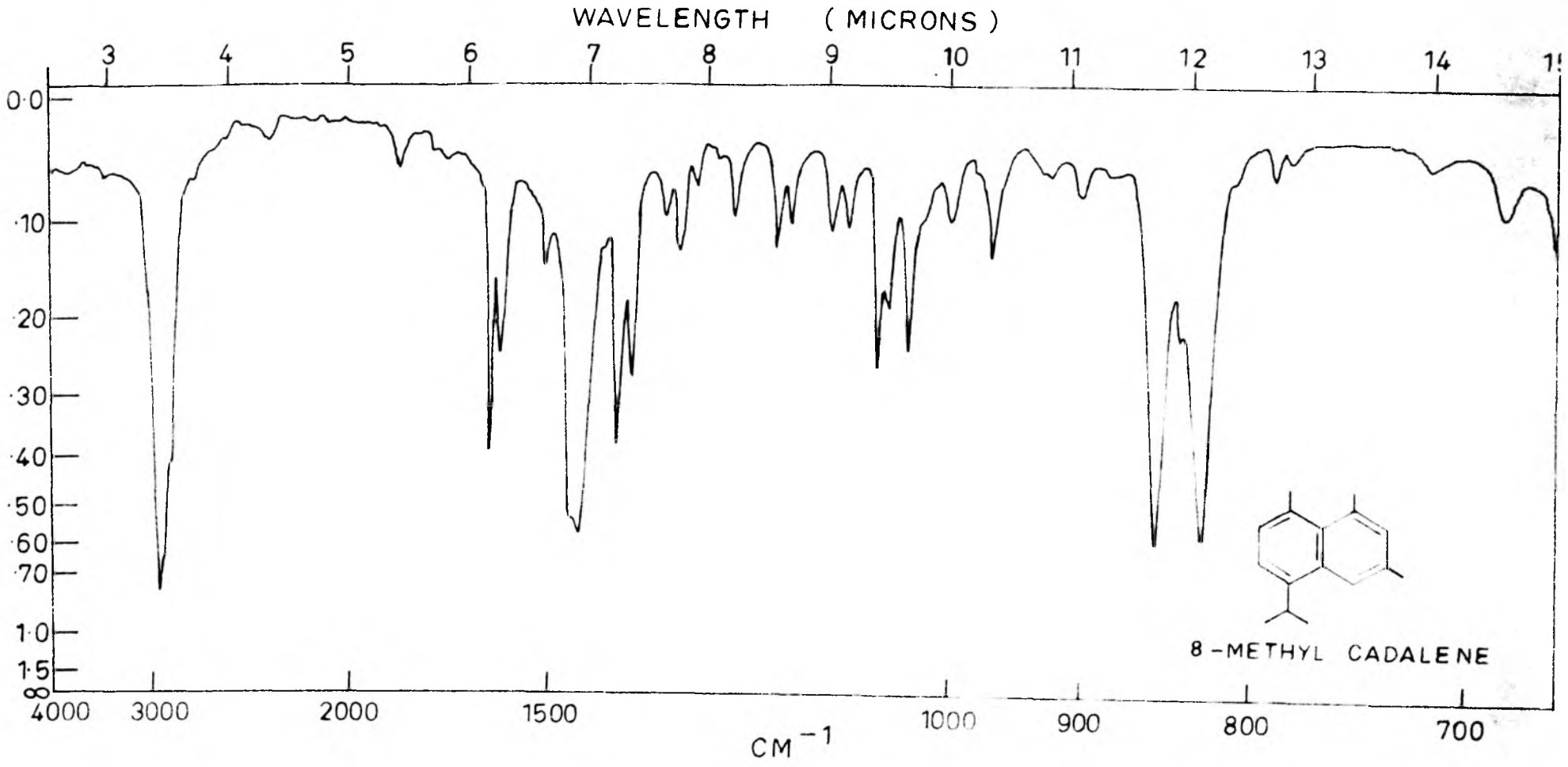
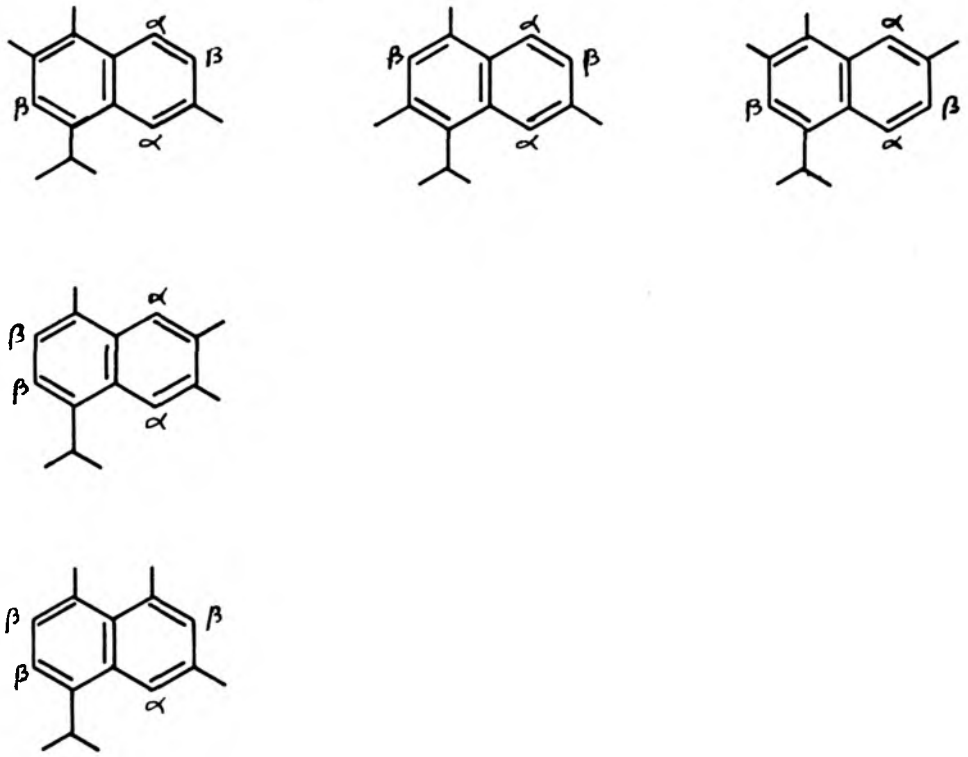


FIG. 7. IR SPECTRUM OF 8-METHYL CADALENE

differentiation within the group of compounds containing two lone hydrogens and a pair of adjacent hydrogens can be made on the basis of whether the hydrogens involved are α or β on the naphthalene nucleus. Thus we have the following subdivision and as can be seen



from Fig.8 the pattern for 2- and 3-methylcadalenes is essentially identical; likewise 1,2,7-trimethyl-4-isopropylnaphthalene which also has the same disposition of hydrogens has essentially the same pattern. 7-methyl and 8-methyl cadalenes which differ slightly in the disposition of the hydrogens have different patterns of absorption in this region. Thus, by making use of absorption in this region it is possible to differentiate all the methylcadalenes

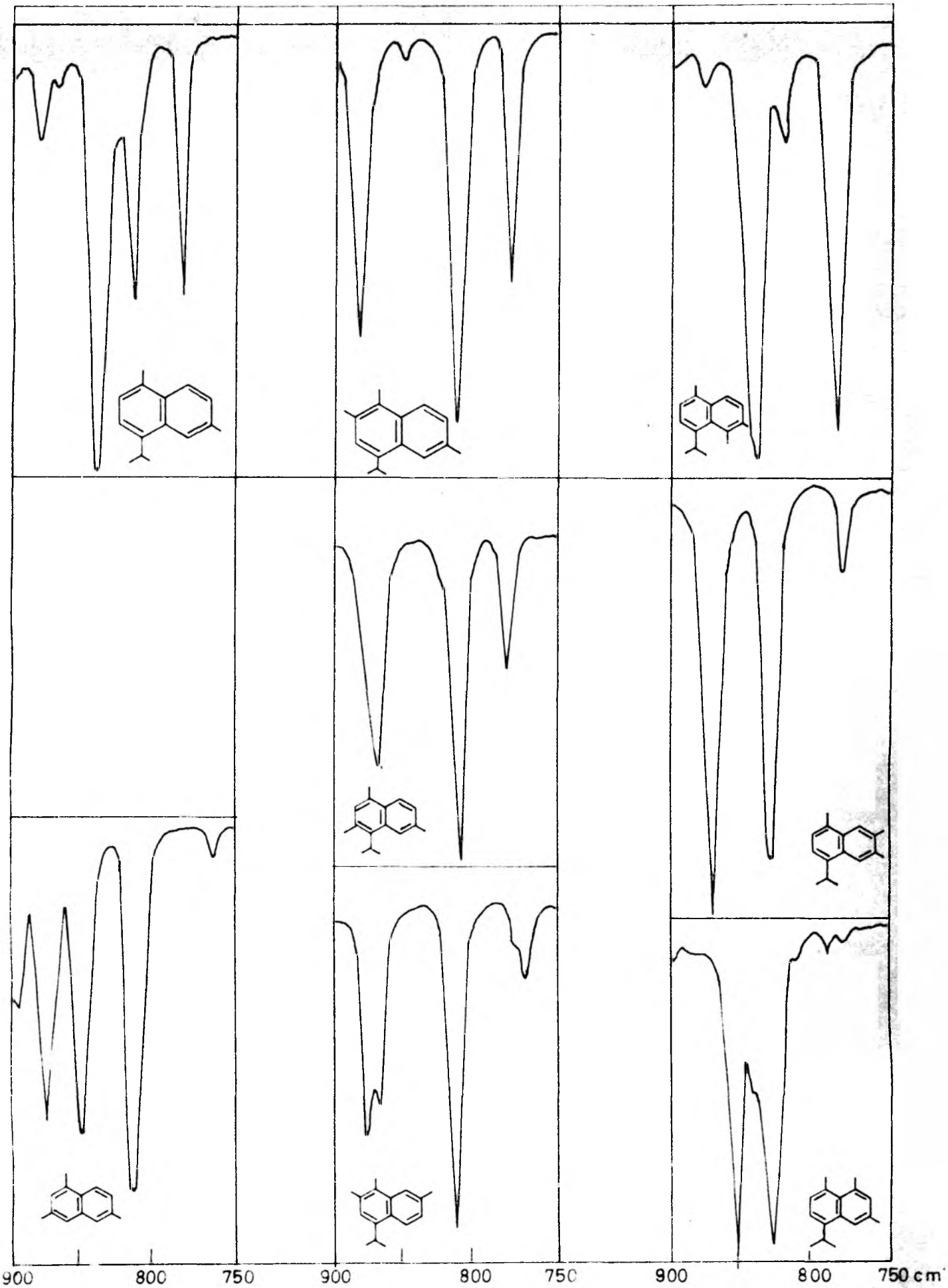
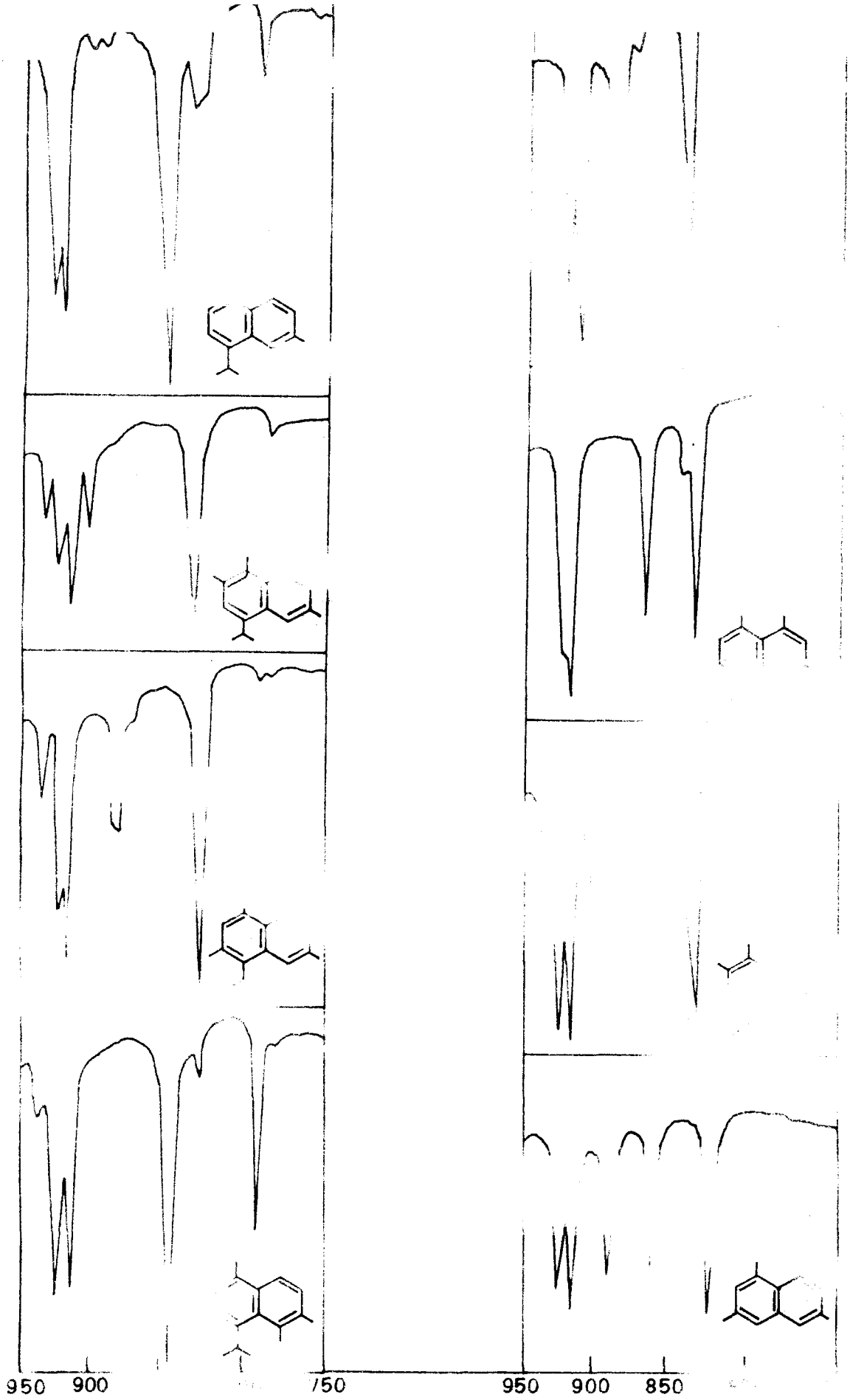


FIG. 8 AROMATIC SUBSTITUTION PATTERNS IN THE 750-900 cm^{-1} REGION

with the exception of 2-methyl and 3-methylcadalenes which though differing from the others cannot be differentiated from each other.

The infrared spectra of the trinitrobenzene complexes of the methylcadalenes have also been studied with a view to see if these complexes can be utilised to identify the substitution pattern by a study of the absorption peaks in the 750-950 cm^{-1} region. The spectra (nujol) of the various TNB adducts clearly showed that the absorption patterns(Fig.9)in the region 750-950 cm^{-1} can be profitably utilised to differentiate all the methylcadalenes. In this region trinitrobenzene has only one strong band at 928 cm^{-1} and this gets slightly modified by interaction with the naphthalene in the complex; the remaining bands are all due to the C-H out-of-plane deformation of the protons on the naphthalene and the overall pattern of the absorption, though remaining the same, the bands suffer a shift ($\sim 14 cm^{-1}$) to the higher frequencies.

1660-2000 cm^{-1} region: Young et al[9] showed that the absorption patterns produced by substituted benzenes in the region 1650-2000 cm^{-1} are typical, within limits, of the types of substitutions and are independent of the nature of substituents. Since then,this region has been used to determine the orientation on the benzene ring by



SUBSTITUTION PATTERNS OF TNB COMPLEXE

several workers[4], and found to be extremely useful. It has been shown by Shiffen[10] that these bands are summation bands (overtone and combination bands) of the C-H out-of-plane fundamentals which occur between 700-1000 cm^{-1}.

Little data are available on the applicability of these absorptions to naphthalenes and Bellamy[4] has suggested that though the patterns in this region may not be helpful in determining the orientation in naphthalenic or polycyclic hydrocarbons, the patterns appear to be quite distinct*.

Fig.10 shows the absorptions in the region 1660-2000 cm^{-1} for the various methylcadalenes, cadalene and 1,2,7-trimethyl-4-isopropylnaphthalene. It can be atonce seen that each compound has given rise to a distinct pattern which can be used with advantage for its identification. However, some regularities regarding substitution may also be noticed. For example, 5-methyl-, 7-methyl-, and 8-methyl-cadalenes which have same type of substitution (i.e. 2,3-hydrogens free) in ring A, show a band around $\sim$ 1850 cm^{-1}; similarly 2-methyl and 3-methylcadalenes and 1,2,7-trimethyl-4-isopropylnaphthalene which have the same type of substitution (2, 4 hydrogens free) in ring B,there

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*Huson and Josien[11] have arrived at the similar conclusion with regard to substituted benzanthracenes.

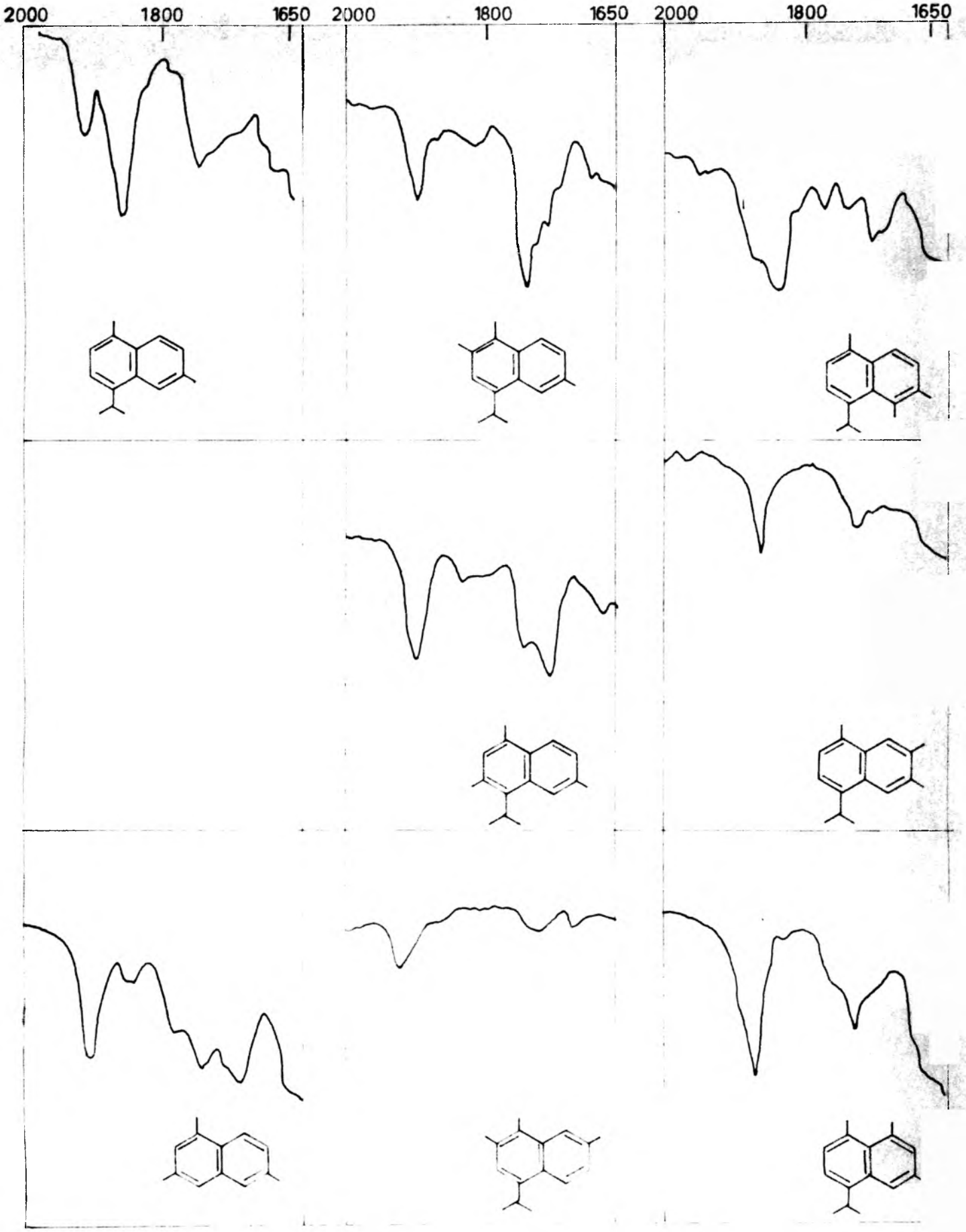

FIG. 10. SUBSTITUTION PATTERNS IN THE 1650-2000 cm^{-1} REGION.

is an absorption peak around ~ 1735 cm^{-1}. It may be noticed further that both these bands are present in cadalene, as might have been expected. Similarly, 1,3,6-trimethylnaphthalene in which ring B has the same disposition as the ring B in cadalene also shows a band at ~1900 cm^{-1} as may be expected in view of the above discussion. It would, thus, appear that this region may in fact prove to be useful for subdividing variously substituted naphthalenes into different classes.

Nuclear Magnetic Resonance (NMR)

Table 2 shows the methyl signals of the various methylcadalenes, cadalene and 1,2,7-trimethyl-4-isopropylnaphthalene. The chemical shift of methyls directly attached to the naphthalene nucleus has been shown to be dependant on its environments and a number of useful rules which help in locating the position of methyls on the nucleus have been suggested[12,13]. The signal due to the isopropyl group in the various cadalenes occurs as a symmetrical doublet (J = 7 c/s) centred at ~ 80 c/s, with the exception of the isopropyl signal in 3-methylcadalene which is centred at 91 c/s. This unexpected shift to lower field strength in the case of 3-methylcadalene could possibly be assigned due to steric factors originating from vicinal substitution.

The aromatic protons of cadalenes form the lowest fieldstrength (415-480 c/s) portion of the spectra. As may

TABLE 2: METHYL SIGNALS OF THE METHYLCADALENES AND SOME OTHER NAPHTHALENIC HYDROCARBONS.

No.	Compound	Methyl signals	
		Aromatic (singlet) in c/s	Isopropyl, 6H doublet centered at c/s (J = c/s)
I	2-Methylcadalene	144, 149, 149	81; (7.5)
II	3-Methylcadalene	146, 150, 152	81; (7.5)
III	5-Methylcadalene	144, 154, 156.5	78.5; (7)
IV	7-Methylcadalene	141.5, 144.5, 154	80.5; (7)
V	8-Methylcadalene	145, 148, 148	79.5; (7)
VI	Cadalene	151, 155	81; (7.5)
VII	1,2,7-Trimethyl-4-isopropylnaphthalene.	145, 149, 149	-

be anticipated, the compounds can be divided into two groups depending on identical orientation in ring A (5-, 7-, 8-methylcadalene) or in ring B (2-, and 3-methylcadalene). The spectra (Fig.11) of the first group are characterised by the presence of a two-proton signal (sharp or a slightly split singlet) at ~ 423-432 c/s and assignable to the two β-protons of ring A*. The remaining aromatic protons in 7-methylcadalene are both α-protons and occur as one-proton signals in the farthest part of the spectrum i.e. 457-465 c/s; practically uncoupled, as the concerned protons are para to each other. In the spectrum of 8-methylcadalene the two protons in ring B are meta to each other and have α-β orientation; in accord with this the β-proton occurs as a broadened siglet at 417 c/s while the α-proton occurs as a similar singlet at 460 c/s; the broadening of these signals is expected as the two protons have a meta relationship ($J_{HH(meta)}$ = 2-3 c/s). The signals due to the protons (α,β) in ring B of 5-methylcadalene may be expected to show an AB type quartet and though this can be recognised in the spectrum, the pattern is complicated possibly due to some unexpected coupling.

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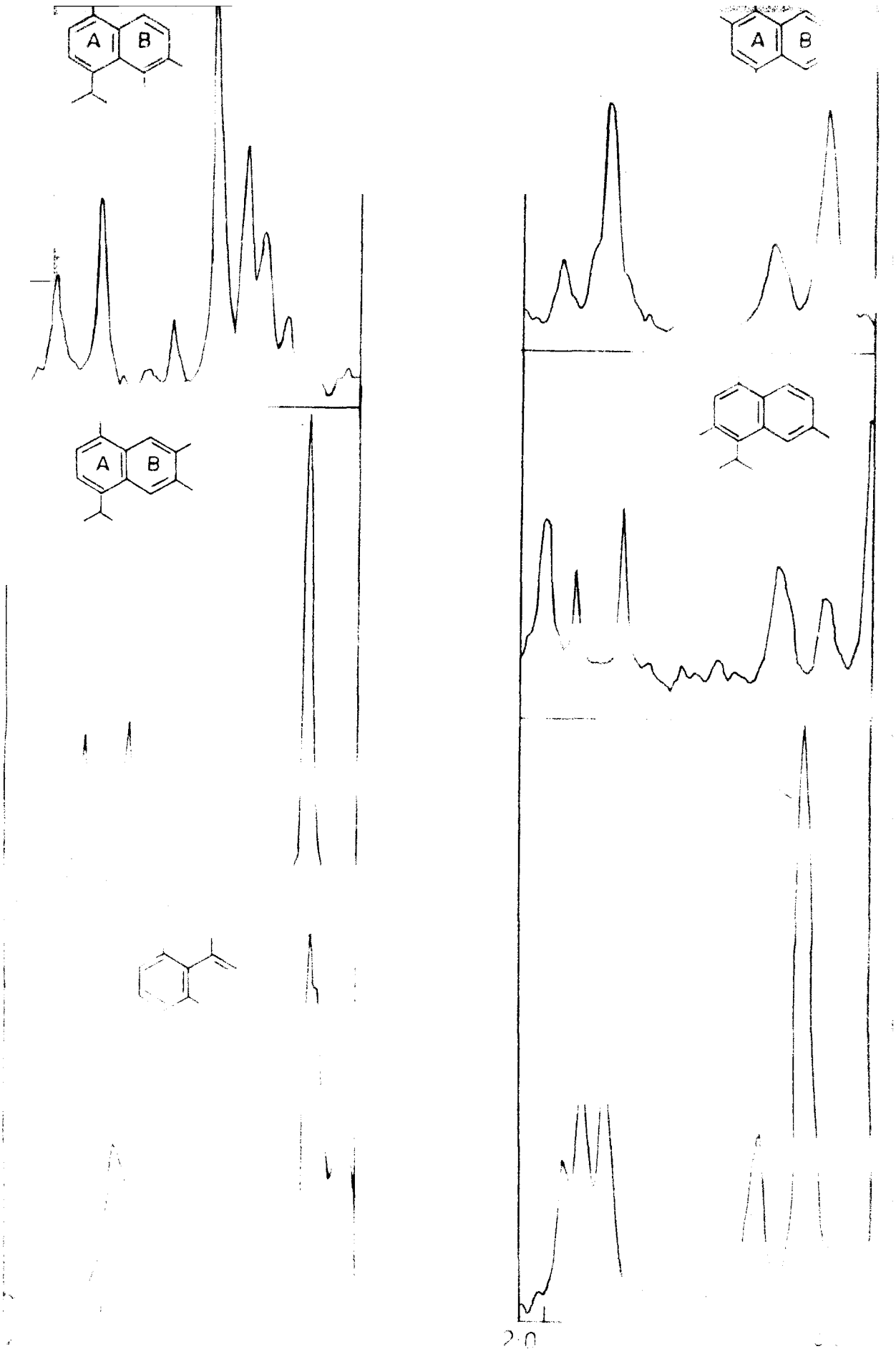
*In naphthalene[14] it has been shown that the β-protons absorb upfield relative to the α-protons and furthermore $J_{\beta\beta}$ is smaller than $J_{\alpha\beta}$.



ON GNAL METHYLCADALENE

In the second group the characteristic two-β-proton signal (β,β) of group A is absent and an AB quartet due to α,β protons in ring B is clearly seen in the spectra of both 2- and 3-methylcadalenes. The α-proton of ring B in 3-methylcadalene occurs at 475 c/s while the β-proton of ring A occurs at 415 c/s. In 2-methylcadalene the α-proton of ring B is overlapping (at 464 c/s) one of the components of the AB quartet while the β-proton of ring A overlaps the signal at 424 c/s.

The spectrum of cadalene has the characteristics expected of both of the above groups.

As can be seen from the above discussion the signals for the various aromatic protons of cadalenes are quite characteristic of each compound and serve as excellent characterising features.

Gas-liquid Chromatography (GLC):

The retention times of various cadalenes have been found (Table 3) to be widely different and this should help in the identification and detection of methylcadalenes, even in a mixture. Fig.12 shows the gas-liquid chromatogram of a mixture of all the cadalenes.

Thin-layer Chromatography (TLC):

Thin-layer chromatography (TLC) of various cadalenes failed to show any difference in the Rf values

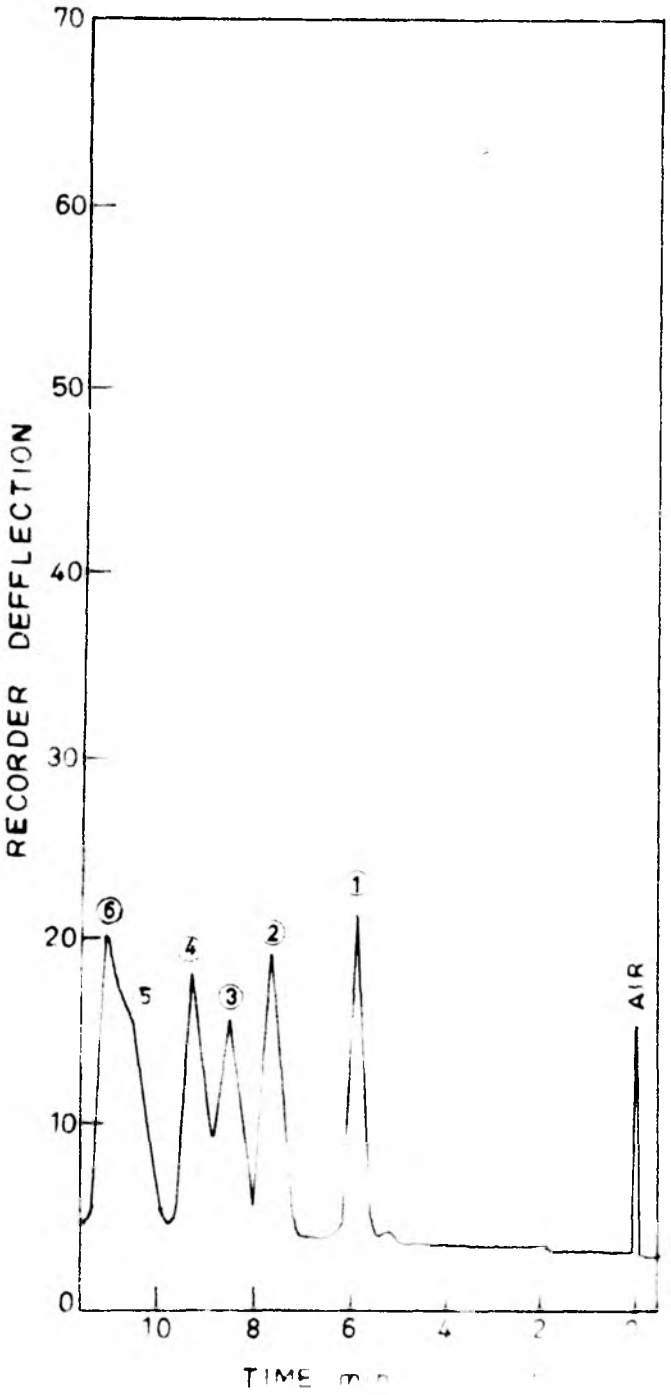
TABLE 3. RETENTION TIME OF METHYL CADALENES

Column	..	P
Temperature		200°C
Pressure	..	25 lbs/sq.in.
Flowrate		
Gas	..	Hydrogen
Recorder range		One
Sample	..	5 ml

Compound	Retention time* cadalene.
Cadalene	1
2-Methylcadalene	1.4285
3-Methylcadalene	1.2557
5-Methylcadalene	1.7714
7-Methylcadalene	1.4858
8-Methylcadalene	1.8285

* $\text{Retention time}_{\text{cadalene}} = \frac{\text{Retention time of the compound}}{\text{Retention time of cadalene.}}$

PERKIN-ELLMER VAPOUR PHASE FRACTOMETER. MODEL 154 D



COLUMN — P
TEMP — 200°
PRESSURE — 25 lbs / sq.in
CARRIER GAS — H_2
RECORDER RANGE — ONE
SAMPLE — 4 µl

1) CADALENE 2) 3-METHYLCADALENE 3) 2-METHYLCADALENE
4) 7-METHYLCADALENE 5) 5-METHYLCADALENE 6) 8-METHYLCADALENE

FIG 12 VAPOUR PHASE CHROMATOGRAM OF THE MIXTURE OF METHYLCADALENE

on silica gel, using petroleum ether. In view of our success[15] in the separation of olefins by taking advantage of their complexing with Ag^+ it was thought worthwhile to see if complexing of an aromatic hydrocarbon with a polynitrocompound could be invoked to effect separation of isomeric aromatic hydrocarbons. For this purpose some preliminary work was carried out with α- and β-methylnaphthalenes using both 2,4,7-trinitrofluorenone and trinitrobenzene in different concentrations, in silica gel, as the other components of the π complex. It was soon concluded from this that the results were better* with TNB and concentration of 10% was adequate. With this procedure some of the cadalenes show distinct differences (Fig.13, Table 4) in the R dye values.

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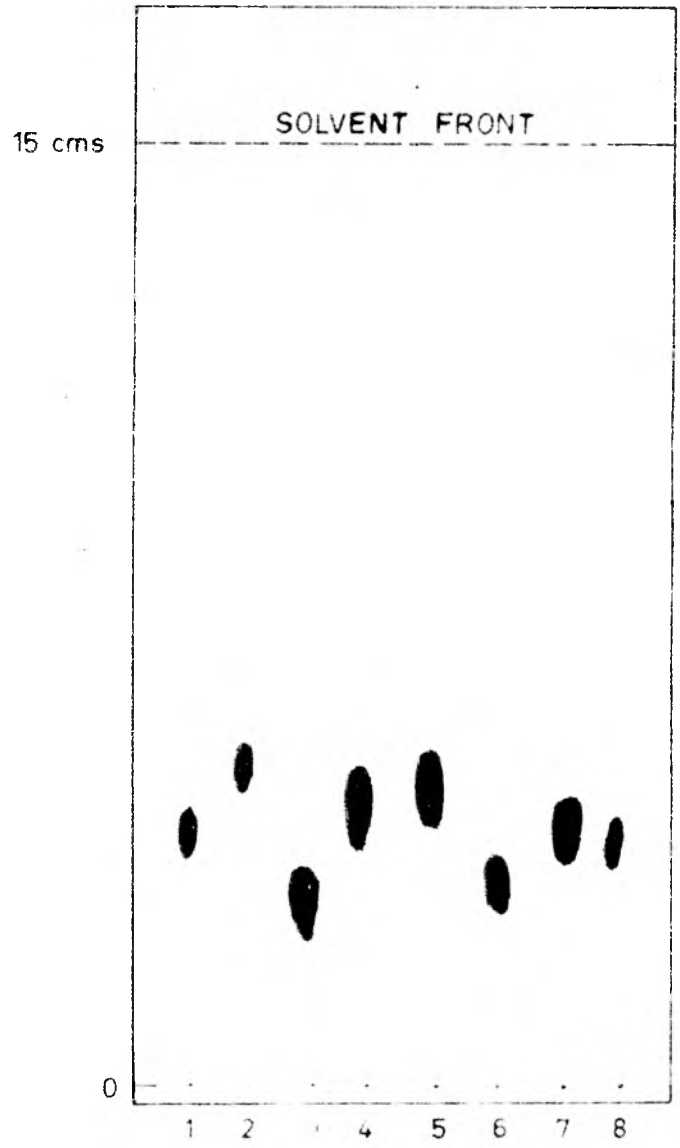
*After the completion of this work two sets of authors[16,17] have reported the separation of polycyclic aromatic hydrocarbons on similar lines. However, these authors did not study the chromatography of isomeric naphthalenes or other isomeric compounds. We find our procedure useful for the separation of various other polycyclic aromatic compounds, but further projected work on the subject has been discontinued in view of the publications mentioned earlier. We find the preparative thin-layer chromatography on impregnated layers useful for separating products of dehydrogenation.

PLATE ---- 10% TNB impregnated silica gel G

SOLVENT SYSTEM --- pet-ether (40-60°)



1) Dye (Azobenzene) 2) Cadalene 3) 2-Methylcadalene

4) 3-Methylcadalene 5) 5-Methylcadalene 6) 7-Methylcadalene

7) 8-Methylcadalene 8) Dye

FIG 13 THIN-LAYER CHROMOTOGRAM OF METHYLCADALENES

TABLE 4. R_{dye} values of Methylcadalenes.

Compound.	R_{dye}^{*}
Azobenzene	1
2-Methylcadalene	0.7968
3-Methylcadalene	1.1875
5-Methylcadalene	1.25
7-Methylcadalene	0.8437
8-Methylcadalene	1.0937

$$R_{dye}^{*} = \frac{R_f \text{ compound}}{R_f \text{ dye}}$$

E X P E R I M E N T A L

Ultraviolet spectra

All UV spectra were measured on a Beckman DK-2 Ratio Recording Spectrophotometer using n-heptane as the solvent.

Concentrations:

Cadalene: A stock-solution was first prepared by dissolving 0.0224 g of cadalene in 10 ml n-heptane. Further the following three dilutions were made for measuring spectrum in different regions.

Dilution	Gm/litre	Region
I	0.0240	340-320 mμ
II	0.0224	320-260 mμ
III	0.00112	250-220 mμ

2-Methylcadalene: 0.0215 g of 2-methylcadalene was dissolved in 10 ml of n-heptane to prepare a stock solution. The following dilutions were made:

Dilution	Gm/litre	Region
I	0.1728	340 - 320 mμ
II	0.01382	320 - 260 mμ
III	0.0008294	250 - 220 mμ

3-Methylcadalene: 0.0170 g of 3-methylcadalene was dissolved in 10 ml n-heptane. The dilutions made were as follows:

Dilution	Gm/litre	Region
I	0.3400	340 - 320 mμ
II	0.01700	320 - 260 mμ
III	0.00068	250 - 220 mμ

5-Methylcadalene: A stock-solution was prepared by dissolving 5-methylcadalene (0.014 g) in n-heptane (10 ml). The following dilutions were made:

Dilution	Gm/litre	Region
I	0.140	340 - 330 mμ
II	0.0140	330 - 260 mμ
III	0.00056	250 - 220 mμ

7-Methylcadalene: 0.0188 g of this hydrocarbon was dissolved in 10 ml n-heptane and thus a stock-solution was prepared. Further the following dilutions were made:

Dilution	Gm/litre	Region
I	0.1880	340 - 320 mμ
II	0.01880	320 - 260 mμ
III	0.001128	250 - 220 mμ

8-Methylcadalene: A stock-solution was prepared by dissolving this hydrocarbon (0.024g) in n-heptane (10 ml). The dilutions made were as follows:

Dilution	Gm/litre	Region
I	0.1992	340 - 320 mμ
II	0.01593	320 - 260 mμ
III	0.0007968	250 - 220 mμ

1,2,7-Trimethyl-4-isopropylnaphthalene: 0.0175 g of this hydrocarbon was dissolved in 10 ml n-heptane. The following dilutions were made:

Dilution	Gm/litre	Region
I	0.1750	340 - 320 mμ
II	0.01750	320 - 260 mμ
III	0.001050	250 - 220 mμ

1,3,6-Trimethylnaphthalene: A stock-solution was prepared by dissolving this hydrocarbon (0.0154 g) in n-heptane (10 ml). The dilutions were made as follows:

Dilution	Gm/litre	Region
I	0.154	340 - 310 mμ
II	0.0154	310 - 250 mμ
III	0.000616	240 - 220 mμ

IR Spectra:

The IR spectra were taken on a Perkin-Elmer Infracord model 137E or on a Perkin-Elmer spectrophotometer model 221 either as smears (liquids) or in nujol (solids). In some cases the IR spectra were taken in a 0.03 mm cell. (neat).

NMR Spectra:

All NMR spectra were taken in ~20% solution in CCl_4 with tetramethylsilane as the internal standard on a Varian A-60 spectrometer; peaks are reported in cycles per second from tetramethylsilane peak.

Gas-liquid Chromatography (GLC)

Gas-liquid chromatography of cadalene, methylcadalenes and some other naphthalenic hydrocarbons was carried out on a Perkin-Elmer Vapour Fractometer model 154-D using column P (succinic polyester of diethyleneglycol on celite). Fig.12 shows the analysis of allthe methylcadalenes.

Thin-layer chromatography (TLC)

Silica gel impregnated with TMB (10%) for the use of TLC was prepared as follows:

To a hot solution of TMB (2.0 g) in ethanol (95%,20 ml) was added silica gel G (20.g Merck quality) and thoroughly mixed. The solvent was evaporated and the impregnated silica gel was dried at $\sim 60^{\circ}$. The dry mixture was finely powdered, mixed with a proper quantity of water and the plates were prepared in the usual way using a spreader. On drying, the plates were activated by heating at $\sim 80^{\circ}$ for 1-1/2 hr, and were thus made ready for use. Azobenzene (3%) was used as a standard dye-solution. After spotting the samples the plate was kept for saturation in the usual manner for 20 minutes. It was developed with pet. ether ($40-60^{\circ}$) upto 15 cms; no spraying with any reagent was necessary as the spots were visible as such.

SUMMARY

UV, Infrared and PMR spectra of methylcadalenes have been studied with a view to effect their characterisation. GLC and TLC of these hydrocarbons have also been investigated and found to be useful for characterisation.

REFERENCES

1 W.L.Mosby, J. Am. Chem. Soc. 75, 3348 (1953)

2 A.E.Bailey, K.C. Bryant, R.A.Hancock, S.H. Morrell and J.C.Smith, J. Inst. Pet. 33, 203 (1947).

3 H.H. Jaffe and M. Orchin, Theory and applications of Ultraviolet Spectroscopy, p.287, John Wiley and Sons Inc. New York (1962).

4 L.J. Bellamy, The Infrared spectra of Complex Molecules p.64, Methuen and Co. London (1958).

5 L. Cencelj and D. Hadzi, Spectrochimica Acta 7, 274(1955).

6 J.G. Hawkins, E.R. Ward and D.H. Whiffen, Spectrochimica Acta, 10, 105 (1957).

7 H.L. Werner, W. Kennard and O. Rayson, Aust. Naturf. J. Chem. 8, 346 (1955).

8 H. Luther and H. Günzler, Z. Naturf 10b, 445 (1955).

9 C.W. Young, R.B. DuVall and N. Wright, Analyt. Chem. 23, 709 (1951).

10 D.H. Whiffen, Spectrochimica Acta, 7, 253 (1955).

11 H. Puson and M.L. Josien, J. Am. Chem. Soc. 78, 3049 (1956).

12 B.A. Nagasampagi, R.C.Pandey, V.S.Pansare, J.R.Prahlad and Sukh Dev, Tet. letters, 8, 411 (1964).

13 F.F.H. Yew, R. Kurland and B.J. Nair, Analyt. Chem. 36, 843 (1964).

14 J.A.Popple, W.G. Schneider and H.J. Bernstein, High-resolution Nuclear Magnetic Resonance, p.147 McGraw Hill Book Co. Inc., New York (1959).

15 A.S.Gupta and Sukh Dev, J. Chromatography 12, 189 (1963).

16 H. Frank-Neumann and P. Jössang, J. Chromatography, 14, 280 (1964).

17 Arne Berg and Jorgen Lam, ibid., 16, 157 (1964).

CHAPTER IV

ELIMINATION OF NON-ANGULAR GROUPS

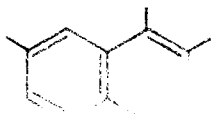
DURING DEHYDROGENATION

ELIMINATION OF NON-ANGULAR GROUPS DURING DEHYDROGENATION

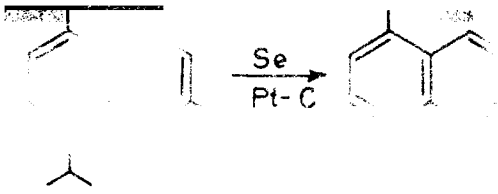
Dehydrogenation, both chemical and catalytic, is a versatile tool for aromatisation of a variety of hydroaromatic compounds; it will be no exaggeration to state that this reaction played a key role in studies of a variety of natural products, especially poly-isoprenoids,[1,2,3] carried out in the 1920 - 1960 period.

Quite early in the studies on dehydrogenation, it was realised that quaternary alkyl groups normally get eliminated during the aromatisation process; ring expansions, ring contractions, ring formation, and migration of alkyl groups have also been often observed[1,2,3].

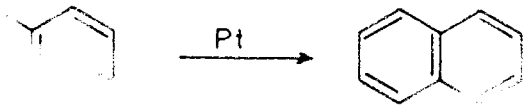
Though, normally, it is only the quaternary alkyl groups which are eliminated, or sometimes migrate during dehydrogenation, elimination (and sometimes migration) of non-angular alkyl groups, especially with selenium, has often been observed. Thus, Ruzicka et al.[4] showed that 1-ethyl-3,4-dihydro-2,7-dimethylnaphthalene (I, Chart 1) was partly converted by selenium dehydrogenation into 2,7-dimethylnaphthalene (II). Cadinene (III) on dehydrogenation with selenium at 320° was shown to afford some 1,6-dimethylnaphthalene (IV) by Diedel and coworkers[5], while Linstead et al.[6] obtained the same compound by heating cadinene with Pt-C at 305°. That 1,2,3,4-tetrahydro-1-



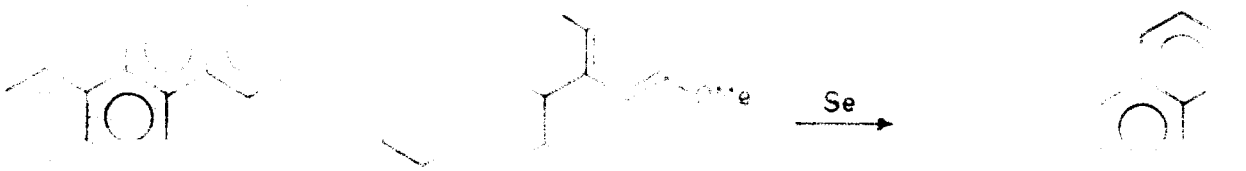
(I)



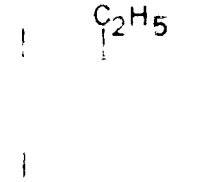
(II) (III)



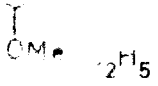
(V)



(VIII) (X)



(XI)



cyclopentylnaphthalene (V) furnished naphthalene (VI) when passed in a current of H_2 over platinum was shown by Haber and his coworkers[7]. Further Jones et al.[8] obtained chrysene (VIII) on heating the perhydrochrysene (VII) with selenium at ~ 300°. Robinson et al.[9] showed that selenium dehydrogenation of compound (IX) afforded 1,2-benzanthracene (X) in a rather poor yield. Cocker and his coworkers[10] reported that 8-ethyl-5,6-dihydro-4-methoxy-1,2-dimethylnaphthalene (XI) furnished 3,4-dimethyl-1-naphthol (XII) on heating the former with selenium at 330°. Further the above authors[10] reported that 4-ethyl-1,2-dihydro-5-methoxy-6,8-dimethylnaphthalene (XIII) yielded 2,4-dimethyl-1-naphthol (XIV) on selenium dehydrogenation.

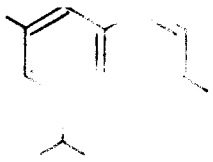
In a detailed study designed to determine the factors responsible for the loss of non-angular alkyl groups in hydronaphthalenes, Cocker et al.[11,12,13] deduced that sulphur-dehydrogenation (~ 230-240°) is normally safe whereas Pd-C (~ 260-80°) as well as selenium (~ 330-50°) encourage dealkylation especially of groups larger than methyl, and in particular when substituted in peri position.

Cocker et al.[11,12,13] used mostly tetralins as the substrate in their studies. In connection with our work described in Chapter II a number of dialins had become available and it was thoughtworthwhile to see if the elimination of non-angular alkyl groups during the aromatisation,

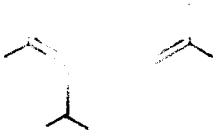
could be a serious side reaction. This study appeared all the more interesting in view of the availability, these days, of the Gas-liquid chromatography (GLC) technique for quantitative determination of the product composition and the availability of Nuclear Magnetic Resonance (NMR) method for establishing the structures of methylnaphthalenes[14,15]. The dehydrogenation of the dialins XV - XX (Chart 2) was investigated with sulphur (305 ± 5°), selenium (305 ± 5°) and 10% Pd-C (260–280°) under identical conditions. The results of these studies have been summarised in Table 1 and 2.

In this study the products obtained by selenium dehydrogenation were separated by preparative GLC and the individual compounds converted into trinitrobenzene (TNB) adducts which were identified either by comparison (mixed m.p., IR and retention time of the naphthalene) with the authentic samples or characterised (i.e. compounds XXII, XXIV, XXVI and XXXIII) by a study of the NMR spectrum of the complex. Table 3 summarises the PMR data of the compounds identified by the latter procedure. The products of Pd-C dehydrogenation were identified by the peak enhancement procedure using authentic samples in mixed chromatograms.

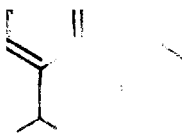
As can be seen from the above results, the dialins covered in Table 1 gave essentially normal products with



(XV)



(XVI)



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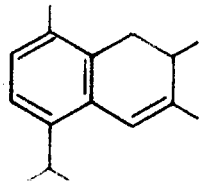
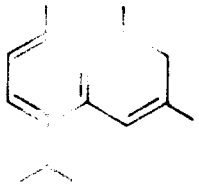


(XVIII)

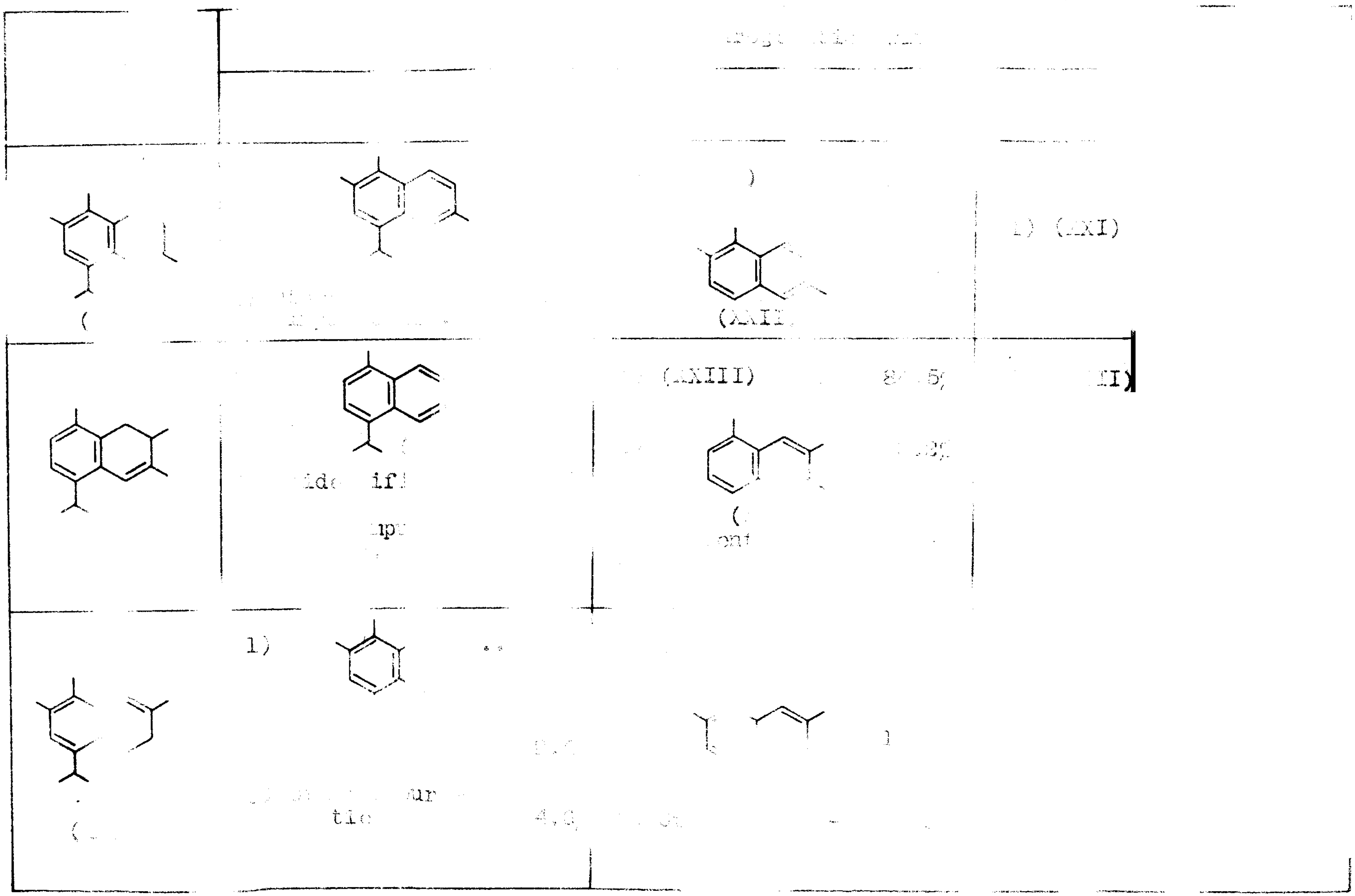


(XIX)

(XX)

CHART - 2

L.



[illegible]BLE 2. [illegible]NGUL[illegible] [illegible]PS D[illegible] [illegible]

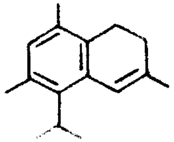
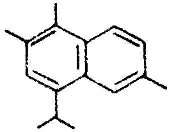
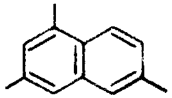
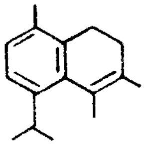
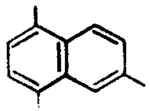
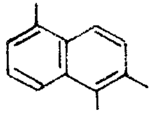
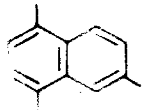
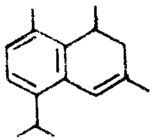
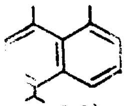
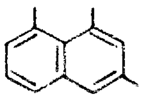
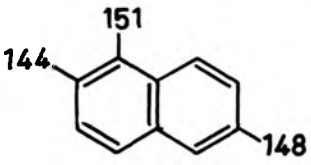
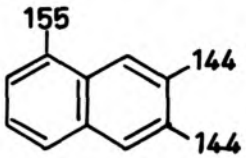
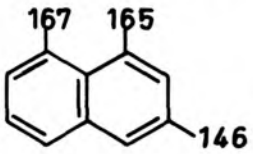
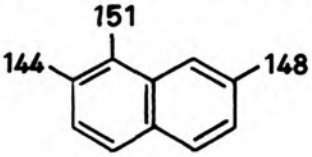
Dialin	[illegible]s	[illegible]roduc[illegible]	[illegible]ge[illegible]	[illegible]h	
	 ([illegible]) 2) Other impurities.	2.5%	 ([illegible]II) [illegible] ied.	8% [illegible]	) (
	 .. [illegible]ies.	91.5%	 .. ([illegible]) 		) (
[illegible]VII) 	 [illegible]II) [illegible]) ..) Oth[illegible] impuri-[illegible]	[illegible]%	 Other impu[illegible]		[illegible]es.

TABLE 3: PMR SIGNALS OF THE TAB COMPLEXES OF THE MINOR PRODUCTS OF DEHYDROGENATION

Starting dialin	Methyl signals (in c/s)		
	Isopropyl groups.	Aromatic methyls.	Structure assigned with predicted values for methyl signals[14].
XV	Absent	148,148,150	
XVIII	"	144,144,154	
XIX	"	142,170,170	
XX	"	146,150,150	

both sulphur and Pd-C and suffered only a minor dealkylation with selenium. On the otherhand, dialins XVI, XVII and XIX (Table 2) suffered extensive dealkylation both with selenium and Pd-C and atleast in one instance (i.e. XIX) some elimination even with sulphur.

Since little is known about the mechanism of dehydrogenation it is difficult to rationalise the above results in terms of a single theory. However, some conclusions can be drawn from the above study and these parallel those deduced by Coozer et al.[11,12,13] in their studies on tetralins.

a) The extent of dealkylation increases in the order S < Pd-C < Se.

b) When a group bigger than methyl is absent either from the ortho or the peri position to a methyl group, little dealkylation occurs even with selenium (cf. Table 1).

c) When the situation described under 'b' no longer obtains, elimination of the bulkier group becomes serious (cf. Table 2). When such groups are located in the periposition the extent of elimination would appear to be much more than when same groups are located ortho to each other. This is vividly demonstrated by the Selenium dehydrogenation of dialin (XVII) when none of 6-methylcadalene is formed. Even when the groups

concerned are methyls but are located in peri-position, elimination could be serious.

E X P E R I M E N T A L

The dialins (XV - XX) obtained during the synthesis of methylcadalenes and some other naphthalenic hydrocarbon were subjected to dehydrogenation with sulphur, selenium and palladised charcoal under the following standard conditions.

1 Sulphur dehydrogenation: Each dialin (~0.5 g) was mixed with theoretical quantity of sulphur and heated at 305 ± 5° for 3 hr under a slight suction (~ 200 mm). The product in each case was directly distilled off over a pinch of freshly precipitated copper powder.

2 Selenium dehydrogenation: A mixture of dialin (~0.5 g) and 1-1/2 times its weight of selenium was heated at 305 ± 5° for 36 hr using an aq-NaOH (20%) trap for the absorption of the liberated H_2Se. The product was then distilled off over a pinch of freshly precipitated copper powder.

3 Palladised-charcoal dehydrogenation: Each dialin (~ 0.5 g) was heated with its equal weight of Pd-C (10%)[16] at 260-80° for ~6 hr during which period a thin stream of carbon dioxide was passed through the system to sweep off the

hydrogen evolved which was collected in a nitrometer. When the evolution of hydrogen ceased (6 hr and practically theoretical quantity of hydrogen was collected in each case), the product was cooled, the catalyst filtered and the residue obtained after the removal of the solvent (pet. ether 40-60°) was distilled over sodium.

GLC analysis:

The products, thus obtained, after all the dehydrogenations were analysed by Gas-liquid chromatography on a Perkin-Elmer Vapour Fractometer Model 154-D under the following identical conditions.

Column: Succinic polyester of diethylene glycol; 25% on celite.
Temperature: 200°
Pressure : 25 lbs/sq. in.
Gas: Hydrogen.
Recorder range : One
Sample : 5 µl

The results of these analyses have been depicted on Table 1 and 2 and Table 4 gives the Retention time* cadalene of the naphthalenes other than methylcadalenes which have already been described in Chapter III.

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*Retention time$_{\text{cadalene}}$ = $\frac{\text{retention time of the compound}}{\text{retention time of cadalene.}}$

TABLE 4: RETENTION TIME OF SOME OF THE NAPHTHALENIC HYDROCARBONS

No.	Compound	Struc. No.	Retention time* cadalene
1	Cadalene	XXI	1.0
2	1,3,5-Trimethylnaphthalene	XXX	1.257
3	1,2,6-Trimethylnaphthalene	XXII	1.028
4	1,2,7-Trimethylnaphthalene	XXVI	0.957
5	1,3,6-Trimethylnaphthalene	XXVIII	0.7856
6	1,3,8-Trimethylnaphthalene	XXXIII	1.214
7	1,6,7-Trimethylnaphthalene	XXIV	0.9428
8	1,2,7-Trimethyl-4-isopropylnaphthalene.	XXV	1.457

*Retention time$_{\text{cadalene}}$ = $\frac{\text{retention time of the compound}}{\text{retention time of cadalene.}}$

Separation of the hydrocarbons by preparative GLC

The products of selenium dehydrogenation were injected separately (0.5 ml ≅ 0.350 g to 0.4 g) on column P (succinic polyester of diethylene glycol on Chromosorb W, 9 ft x 1") at 200° using nitrogen (15 lbs/sq. in.) as the carrier gas. Fractions corresponding to the peaks in GLC were collected separately in receivers maintained at ~ -10°.

Trinitrobenzene complex of each of the fraction collected above was prepared in the usual manner and the TNB complexes were crystallised from 90% acetic acid. The following Table 5 summarises m.pt. data of these derivatives (other than methylcadalenes).

TABLE 5: MELTING POINTS OF THE TNB DERIVATIVES OF SOME ALKYLNAPHTHALENES

No.	TNB Derivative of	Melting point	
		Present sample.	Reported[17]
1	1,2,5-Trimethylnaphthalene	158.5 - 160°	159-60°
2	1,3,6-Trimethylnaphthalene	142-43.5°*	147-48°
3	1,2,7-Trimethylnaphthalene	141-43°	145-46° 147-48°
4	1,3,6-Trimethylnaphthalene	148-50°	-
5	1,3,8-Trimethylnaphthalene	138-40°	-
6	1,6,7-Trimethylnaphthalene	133-35°*	142-43°
7	1,2,7-Trimethyl-4-isopropylnaphthalene.	134-35.5°	-
8	Cadalene	108-10°	112-13°[18]

*As compounds obtained were very little in quantity, further crystallisations could not be tried.

PMR spectra of the TNB complexes:

All the PMR spectra of the TNB derivatives of methylnaphthalenes were taken in a ~ 2-5% solution in CS_2 with tetramethylsilane as the internal standard on a Varian Associates A-60 spectrometer; peaks are reported in c/s values (Table 3).

SUMMARY

Dehydrogenation of various dialins described in Chapter IV have been studied with S, Se and Pd-C to collect information on the extent of elimination of non-angular alkyl groups.

REFERENCES

1 P.A. Plattner in Newer Methods of Preparative Organic Chemistry, p.21, Interscience, New York (1948).

2 G. Chiurdoglu and M. Descamps, Industrie Chimique Belge, 33 (1961).

3 Z. Velanta in Elucidation of Structures by Physical and Chemical Methods (Technique in Organic Chemistry, Edited by A. Weissberger) Vol.IV, Part I, page 581, Interscience, New York, London (1963).

4 L. Ruzicka, L. Ehmann and E. Mörgeli, Helv. Chim. Acta, 16, 325 (1933).

5 C.F. Siedel, P.H. Müller and H. Schinz, Helv. Chim. Acta. 27, 738 (1944).

6 R.P. Linstead, K.G.A. Michaelis and S.L.S. Thomas, J. Chem. Soc. 1139 (1940).

7 Ya. I Denisenko and A.D.Gabor, J. Gen. Chem. (U.S.S.R.) 10, 193-201 (1940); Chem. Abs. 40, 7283 (1940).

8 W.E. Jones and G.R. Ramage, J. Chem. Soc. 1853 (1935).

9 J.W. Cook and (Mrs) A.M. Robinson, ibid. 505 (1938).

10 W. Cocker, B.E. Cross, A.K. Fateen, C. Lipman, E.R.Stuart, W.H. Thompson and D.R.A.Whyte, ibid. 1781 (1950).

11 W.S. Cocker, B.E.Cross and (Miss) J. McCormick, ibid., 72 (1952).

12 W. Cocker, B.E.Cross, J. T. Edward, D.S.Jenkinson and (Miss) J. McCormick, ibid. 2355 (1953).

13 W. Cocker and D.S. Jenkinson, ibid., 2420 (1954).

14 B.A.Nagasampagi, R.C.Pandey, V.S.Pansare, J.R.Prahlad and Sukh Dev, Tetrahedron Letters 8, 411 (1964).

15 F.F.L. Yew, R. Kurland and B.J. Mair, Analyt. Chem. 36, 843 (1964).

16 Organic Syntheses Coll. Vol.3, p.685, John Wiley and Sons, New York (1955).

17 Faraday Encyclopedia, Hydrocarbon compounds C_{1-3} (compiled by J.E. Faraday) Vol.12, Butterworth Scientific Publications, London (1956).

18 P.A. Plattner and G. Magyar, Helv. Chim. Acta, 24, 131 (1941).

Part Two

CHEMICAL EXAMINATION OF THE WOOD

FROM CEDRELA TOONA

C O N T E N T S

CHAPTER I

INTRODUCTION

MELIACEAE FAMILY AND CHEMOTAXONOMY

MELIACEAE FAMILY AND CHEMOTAXONOMY

INTRODUCTION

MELIACEAE is one of the important families yielding valuable timbers of the world. The famous timbers of the world[1] like the toon of India, cigarbox cedar of tropical America, the calantas of Phillipines, the Australian rose woods and many mahoganies of Africa belong to this family. Species belonging to this family are normally restricted to tropical regions of the world with a few ones extending to subtropical and temperate regions.

Meliaceous woods[2] are generally reddish-brown in colour and often possess some aromatic odour. They hold their important place in the furniture and cabinet trade as they can be seasoned easily and worked readily under tools. They are quite durable and are not subject to much shrinkage. Most of them are reputed as resistant to insect-attack and to possess medicinal properties[3].

In the systematic botanical classification Meliaceae is placed[4] as shown below:

Division	:	Trachaeophyta
Sub-division	:	Pteropsida
Class	:	Angiosperms
Sub-class	:	Dicotyledonea
Order	:	Geraniales (21 families)[5,6]
Family	:	MELIACEAE

Further, Meliaceae family consists[7] of fifty genera and about one thousand species occuring as trees, shrubs and woody herbs. Thus if some are of commercial importance others are grown ornamentally. Of the fifty genera only nineteen genera[8] are reported to occur in India and these are:

1	Aglaia Lour	11	Lansium Rumph
2	Amoora Roxb.	12	Melia Linn.
3	Azadirachta A. Juss	13	Munronia Wight
4	Cedrela Linn.	14	Sandoricum Cav.
5	Chisocheton Blume	15	Soymida A. Juss.
6	Chloroxylon D.C.	16	Swietenia Linn.
7	Chukrassia A. Juss.	17	Turrea Linn.
8	Cipadess Blume	18	Walsura Linn.
9	Dysoxylum Blume.	19	Xylocarpus Koen.
10	Heynea Roxb.		

Of these, so far, the chemical examination of only some species of eleven genera has been done in any detail. These will now be very briefly reviewed.

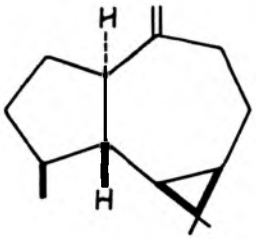
CHEMICAL CONSTITUENTS

1 Genus: Aglaia Lour (125 species...about 20 in India)

Species: Aglaia odoratissima (Sanskrit: Priyangu)

This plant occurs[9] on the hills of Mount Abu, Western ghats and in Kerala State. The fruit is edible and possesses cooling and astringent properties. It is used as a tonic and in inflammation.

The essential oil obtained by the steam-distillation of the seeds was examined by Baslas[10] and it has been shown to contain aromadendrene (I,~ 50%)*, cineol (~ 10%), α-terpinene (II,~ 12.5%) and citral (~ 7%). The fatty acids[11] also have been isolated from the seed-oil and identified by the same author.



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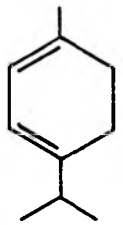

II

2 Genus: Amoora Roxb. (35 species...12 species in India)

Species: Amoora rohituka (Sanskrit: Rohitaka, Hindi: Harinhara)

Amoora rohituka[12] is a middle-sized evergreen tree commonly met within various parts of India and more particularly in Assam, Oudh and Western ghats of India. The bark of this plant is used as an astringent. The oil obtainable from the seeds is used as a stimulating liniment in rheumatism.

The oil obtained by the solvent extraction of the seeds has been examined by three groups[13,14,15] of workers.

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*The structures given in this article represent the absolute configurations, if known.

Thus Patwardhan *et al.*[13] have isolated and identified the fatty acids present in it while M. Hosain *et al.*[14] have reported the isolation of fatty acids together with a sterol (m.p. 135°) and an essential oil.

3 Genus: *Azadirachta A. Juss.*

Species: *Azadirachta indica* syn *Melia azadirachta*

(Sanskrit: *Nimba*; Hindi: *Nim*)

Azadirachta indica[16] known as the Indian Lilac is a moderately tall tree attaining the height of about 40-50 ft. and is normally found in all parts of India. All the parts of this plant except the wood have medicinal properties. Thus the root bark, stem bark and young fruits are used as tonic and antiperiodic. The oil, nuts and leaves act as local stimulant, insecticides and antiseptic. The flowers, gum, and toddy are used as tonic.

Watson and his coworkers[17] in 1923 reported the isolation of some bitter principles from the neem oil. Later on systematic investigations initiated by Siddiqui *et al.*[18-21] resulted in the isolation of a number of bitter and non-bitter principles from the different parts of the tree. Thus, from the neem oil[18] two crystalline bitter principles nimbin, nimbinin, an amorphous neutral bitter principle nimbidin and a sulphur containing compound named nimbidiol were isolated. From the blossoms[19] β-sitosterol (nimbosterol), β-sitosterol glucoside (nimbosterin), nimbicetin, an essential oil, a saturated hydrocarbon

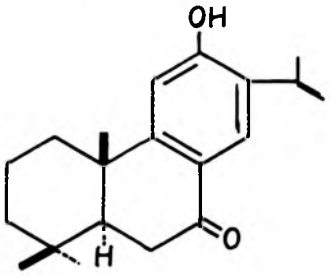
nonakosane and some fatty acids were isolated. Further the same authors reported the isolation of nimbin, nimbinin, nimbidin, β-sitosterol and a mixture of fatty acids from the trunk bark[20]. Finally, the rootbark[21] was shown by the above authors to be containing nimbin, nimbidin and β-sitosterol (nimbosterol).

The fatty acids[22] of the neem oil and the colouring matters[23] from the flowers, identified as flavonoids myrcetin, quercetin and kaempferol have been isolated by Seshadri and coworkers. It has been shown by them that the above colouring matters exist as their 3-glucosides.

The neem gum has been shown to yield after hydrolysis, aldobiuronic acid, L-arabinose, L-fucose, D-galactose and D-glucuronic acid by Mukherjee et al.[24].

Sengupta and his coworkers[25] re-examined the constituents of the trunk bark extract by isolating both bitter and non-bitter principles. The bitter principles consisted of nimbin and nimbiol, whereas, the non-bitter principles were identified as sugiol (III), a paraffin alcohol and β-sitosterol. They further showed that the so-called nimbosterol of Siddiqui et al.[19-21] was nothing but β-sitosterol. Based on the chemical and spectral data the above authors assigned the structure (IV) to nimbiol, the methyl ether of which was synthesised, later on, by three different groups[26,27,28] of workers. The synthesis of nimbiol has been achieved by Wenkert et al.[29].

The molecular formula of the bitter principle nimbin had remained as a controversial problem till recently when Narayanan et al.[30] assigned the correct molecular formula as $C_{30}H_{36}O_9$ based on the elemental analysis, mass and NMR spectroscopic methods. Further, both chemical and spectroscopic evidences have led them[30] to assign tentatively the structure (V) to nimbin.



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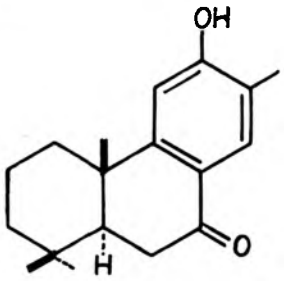

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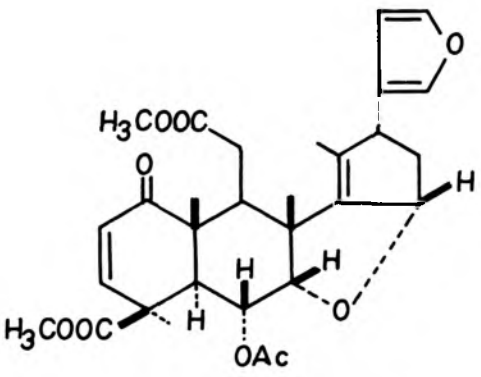

V

4 Genus: Cedrela Linn. (18 species....5 species in India)

Species: Cedrela toona (Sanskrit: Nandi vriksha; Hindi: Tun)

This[31] is a large deciduous tree generally found in many parts of India. The bark of the tree is reputed as a powerful astringent and antiperiodic. It is used for chronic infantile dysentery and as an external application for ulcers.

The flowers are emmenagogue.

The colouring matters of the flowers were first studied by Perkin[32] who identified them as mycanthin, quercetin as its glucoside and an unidentified flavone.

Pillai *et al.*[33] examined the essential oil obtained by the steam-distillation of the wood and showed that it consisted of l-copaene (VI)*, l-cadinol, cadinene and some bicyclic sesquiterpenes.

The isolation of a lactone named as cedrelone, a colouring matter, and an essential oil by the solvent extraction of the wood powder was reported by Parihar and Dutt[34]. However, their investigations on all the above three remained inconclusive. The chemistry of cedrelone has recently been studied completely by Govindachari *et al.*[35] and Raphael and co-workers[36]. Chemical evidences supported by the NMR data and X-ray crystallographic studies have led them[36] to assign structure (VII) to cedrelone.

Seshadri and co-workers[37] have isolated a leucocyanidin from the wood extract and the structure (VIII) has been assigned to it.

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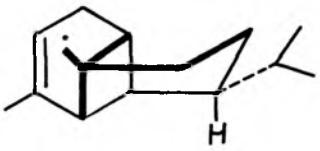
*See Chapter III for its structure determination.



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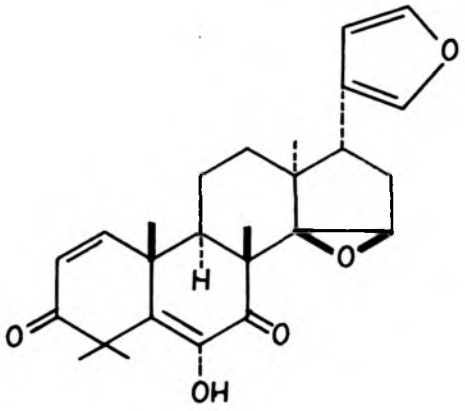

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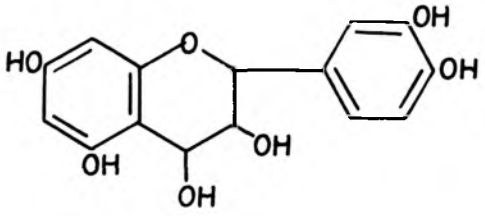

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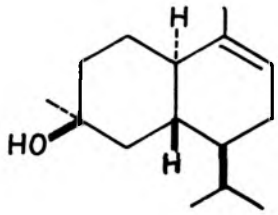


IX

2 Species: Cedrela odorata

Cedrela odorata is a valuable timber tree of tropical America. A sesquiterpene alcohol identified as δ-cadinol[38] (IX) has been isolated by Chierdoglu et al.[38a].

5 Genus: Chloroxylon D.C.

Species: Chloroxylon swietenia (Hindi: Bhoura)

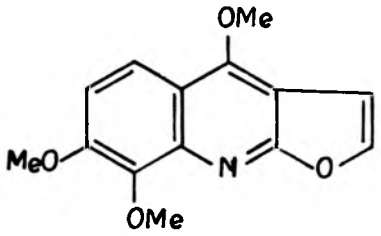
This[39] is a moderate-sized tree commonly found in the Western ghats. The bark is used as an astringent. The leaves are applied to wounds and also prescribed in rheumatism.

An alkaloid named, chloroxylonine, was isolated from the bark of this species by Auld[40] in 1909. Later on Mookerjee et al.[41] using a simpler method isolated from the

bark an alkaloid and a bitter crystalline substance. Further, the alkaloid was shown to be identical with skimmianine (X).

King et al.[42] have reported the isolation of three coumarin compounds by the solvent extraction of the heartwood. Those three compounds have been identified by them as xanthyletin (XI), xanthoxyletin (XII), and 7-demethyl suberosin (XIII).

The fatty acids of this species have been isolated and identified by Rau and Simonsen[43].



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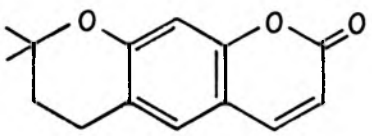

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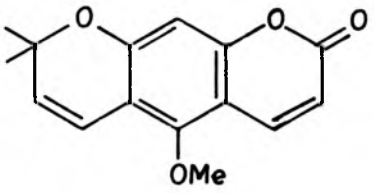

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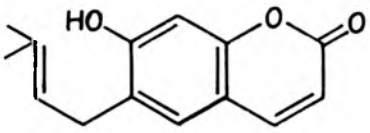


XIII

6 Genus: Dysoxylum Blume (12 species in India)

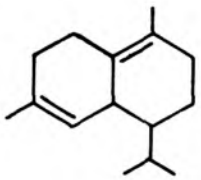
Species: 1) Dysoxylum spectabile, Hook

By the solvent extraction of the heartwood Cambie[44]

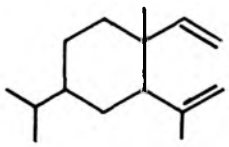
has isolated two compounds identified as β-sitosterol and catechin.

Species: (2) Dysoxylum frazeranum

A cadinenic sesquiterpene dysoxylonene[45] has been isolated and shown to be (±) δ-cadinene (XIV). Very recently, another sesquiterpene hydrocarbon named δ-elemene[46] has been isolated and on the basis of the spectral and degradative studies, structure (XV) has been advanced for it.



XIV



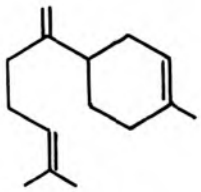
XV

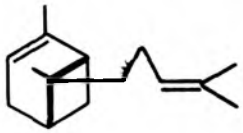
7 Genus: Lansium Rumph (3 species in India)

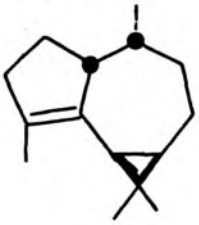
Species: Lansium anamalayanum (Kannada: Chigadmari; Malayalam: thevathali)

This[47] is a medium-sized tree found in the Western ghats of Kanara, Wynad and Kerala. Jois et al.[48] were the first to obtain an essential oil from the wood by steam-distillation. Later on Guha and co-workers[49] reported the isolation of bisabolene and two other unidentified sesquiterpene hydrocarbons. Recent repetition of their work[50] in this Laboratory has revealed that the essential oil consists of β-bisabolene

(XVI), ∝-bergamotene (XVII) and ∝-gurjunene (XVIII).







(XVI) (XVII) (XVIII)

8 Genus: Melia Linn. (2 species in India)

Species: Melia azedarach (Sanskrit: Mahanimba; Hindi: Bakayan)

The occurrence[51] of this tree is normally restricted to the Kashmir area. The flowers and leaves are used to relieve nervous headaches. The flowers are also used as a vermicide and in erruptive skin diseases. The juice of the leaves is said to be anthelmintic, antilithic, diuretic and emmenagogue. The leaves and the bark are used internally and externally in leprosy and scrofula. The root bark is used as an anthelminitic.

Kafuku et al.[52] isolated some fatty acids, a phytosterol and a mixture of hydrocarbons from the oil obtained from the seeds. Siddiqui and his co-workers[53], later on, reported the isolation of an amorphous bitter principle named as bakayanin from the pericarp of the fruit. Apart from this they isolated a non-bitter acidic fraction, bakayanic acid and a sterol.

A crystalline compound possessing the antheimintic properties similar to santonin has been shown to be present in the bark extract by Nakabayashi[54].

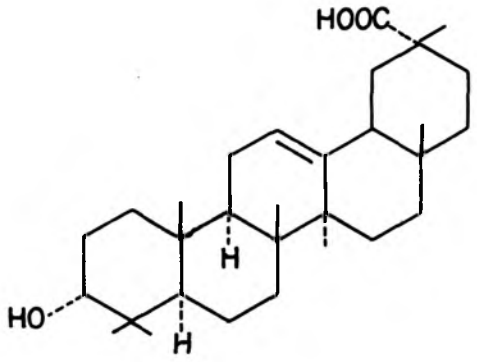
From the wood extract a lactone named bakalactone, a sweetsmelling oil, a resinous product and tannis have been isolated by Bholanath[55].

3 Genus: Sandoricum Cav. (1 species in India)

Species: Sandoricum indicum.

This[56] is an evergreen tree occuring in most parts of India. The roots are used as a carminative and in cases of diarrhoea and dysentery.

The isolation of a major triterpene acid named Katonic acid and a minor acid, indicic acid, from the heart-wood extract of Sandoricum indicum, has been reported by King et al.[57]. Katonic acid has been converted to β-amyrin and its derivatives thus showing that it belongs to the β-amyrin group of triterpenes. Based on the chemical evidence, structure (XIX) has been assigned to it. The minor acid, indicic acid, has been further shown to be an ester of Katonic acid in which the 3-hydroxy group is combined with an unidentified triterpene.



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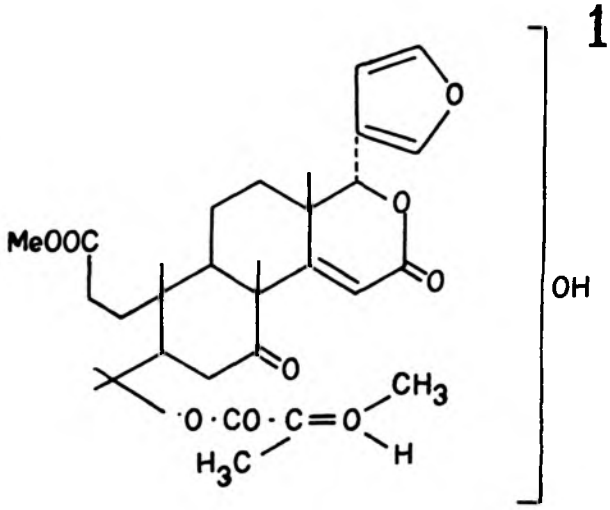

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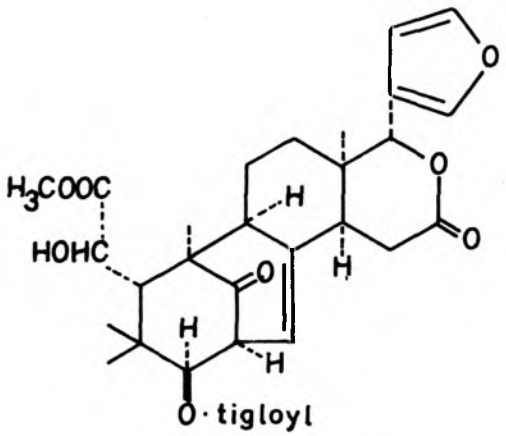


XXI

10 Genus: Swietenia Linn.

Species: Swietenia macrophylla

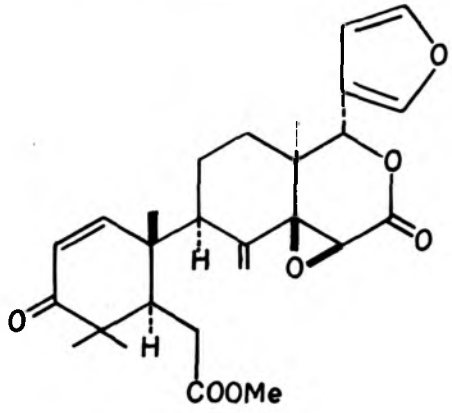
Guha Sircar[58] isolated from the seeds of Swietenia macrophylla a bitter and a non-bitter principle named as swietenolide and swietenine respectively. Some structural investigations were carried out by Chatterjee and co-workers[59] and the structure (XX) was proposed for swietenine tentatively. But the recent X-ray crystallographic studies on swietenine coupled with the NMR data and chemical evidences have led Overton et al.[60] to advance the structure (XXI) for swietenine tentatively.

11 Genus: Xylocarpus Koen. syn Carapa Aubl. (2 species in India).

Species: Carapa guianensis syn Xylocarpus guianensis

Carapa guianensis is a large tree of the equatorial forests of South America and the Goldcoast of Africa.

The isolation of a triterpene andirobin from the seeds of Carapa guianensis has been reported by Ollis et al.[61]. Based on the chemical and spectral data structure (XXII) has been assigned tentatively to andirobin. The co-occurrence of another triterpene identified as 7-deacetoxy-7 ketogedunin (XXIII) with andirobin, has also been reported by the above authors.



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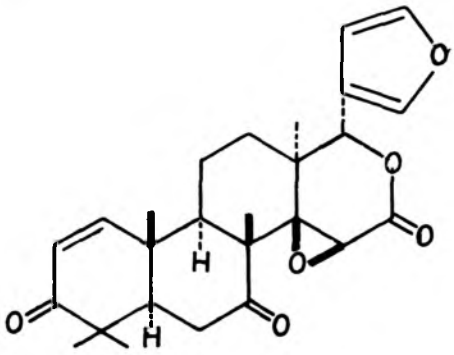


XXIII

CHEMOTAXONOMY

The remarkable progress in the field of the chemistry of natural products, marked by the isolation, from plants, of a number of natural products and their structure elucidation has inspired Organic Chemists to study the

interesting relationship between plant constituents and plant classification i.e. Chemotaxonomy. Chemotaxonomy has been defined[62] as the distribution of chemical compounds or groups of biosynthetically related compounds in series of related or supposedly related plants.

A systematic chemical examination of the constituents of the different genera of the same family and also of related families may establish a relationship between the Botanical plant classification and plant constituents. Botanical classification is normally based on morphology whereas the plant constituents are dependant on physiology with which the biosynthesis is concerned. Both morphology and physiology[63] are controlled by genetic factors which act through enzyme systems. Further, if morphology is controlled in a rather complex way than the physiology which appears to be simple as it is more concerned with the biosynthesis of chemical constituents with molecular characteristics such as terpenoids, steroids, flavonoids and alkaloids. The biosynthesis is further controlled at every stage by enzyme systems.

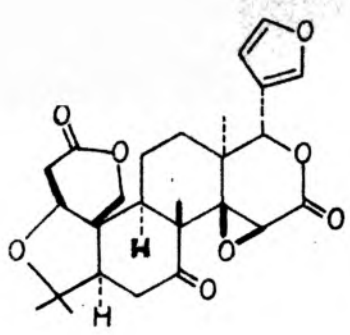
Thus, if genetic factors produce a particular morphological pattern in different genera of the same family, one may expect same or related compounds in all the different genera because similar enzymatic systems in related plants should produce analogous compounds. But

it cannot by any means become a general rule because compounds like fatty acids, amino acids and sugars occur in most of the plants. Why, even certain compounds may be missing from the individuals of the same species or may occur in different percentages. This has been found to be the case during our chemical examination of two individuals of the species of Cedrela toona of different origins. The reason for these changes may be attributed to the effect of soil and climatic conditions. However while comparing the constituents of different genera of a given family some compounds may be missing but the ones which are present may help providing a link between them.

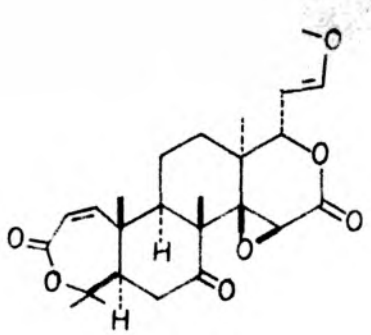
The principle of chemotaxonomy has been successfully applied by Prof. Erdtman[64] during his investigations on the constituents of Conifers. The modern taxonomic studies are founded in the tendency to make phylogeny (the evolutionary development) the basic principle of taxonomy. An application of the principles of chemotaxonomy or phylogenetic relationship to the Meliaceae family may be considered now.

Chemotaxonomy and Meliaceae family

Meliaceae is considered to have been derived[65] from Rutaceae which belongs to the same Natural Order Geraniales as Meliaceae. The bitter principles[66] namely limonin (XXIV) obacunone (XXV) and nomilin (XXVI) isolated from the same



XXIV



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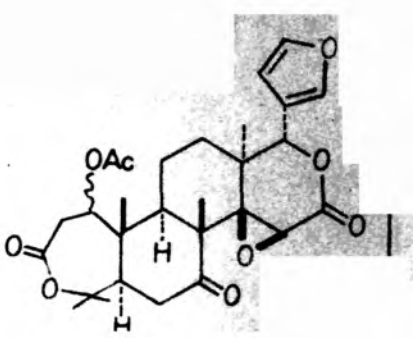

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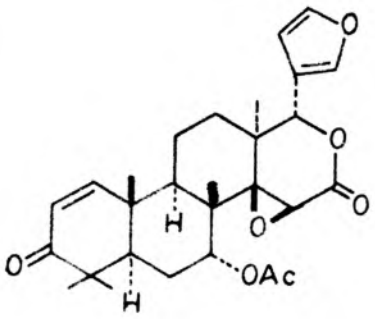
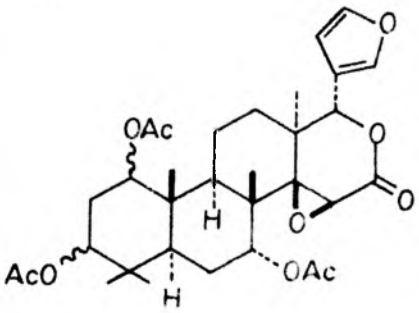
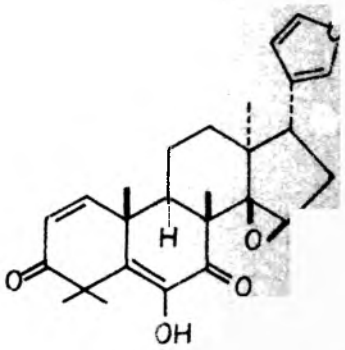


XXVII



XXVIII



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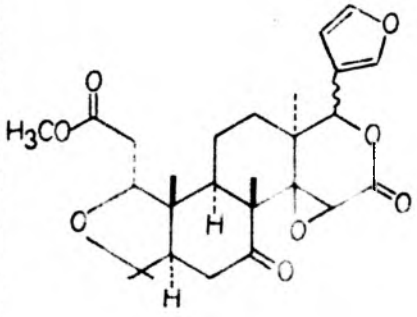
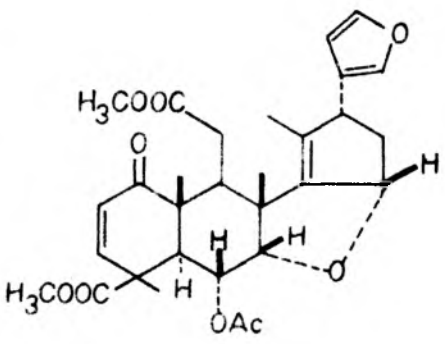


XXIX



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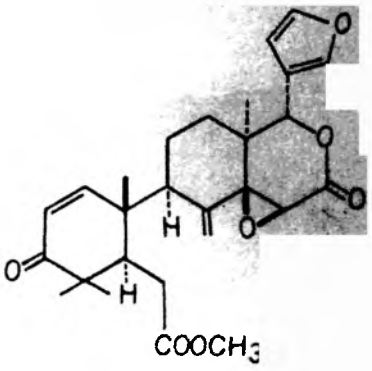

XXII

CHART 1 – LIMONIN AND RELATED COMPOUNDS

citrus species of the Rutaceae family* were shown to be related with one another both chemically and biogenetically. Further the constituents namely gedunin (XXVII)[67] and khivorin (XXVIII)[68] isolated from the species of West African genera Entandophragma and Khaya respectively of Meliaceae family[68a] have been shown to be related with the above limonin group of triterpenes. It is clear that gedunin is at a lower oxidation level than limonin. More recently cedrelone[35,36] (VII) isolated from Cedrela toona (Meliaceae), nimbin[30] (V) isolated from Melia azadarchta and andirobin[61] (XXII) isolated from Carapa guainensis have been added to the list of limonin and related compounds.

Thus, all the above compounds viz. limonin, obacunone, nomilin, gedunin, khivorin, cedrelone, nimbin and andirobin belong to the class of skeletally related C_{26} modified triterpenoids of the euphol type. Except nimbin and andirobin, all the remaining compounds have in common a number of structural features such as a β-substituted furan ring, a β-epoxide function involving C_{14} and C_{15} a β-methyl at C_8 and an oxygen substitution at C_7. The D ring in both cedrelone and nimbin is intact in contrast to the other members of the series whereas the C ring in

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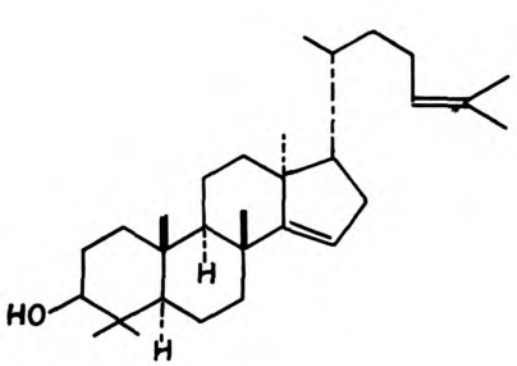
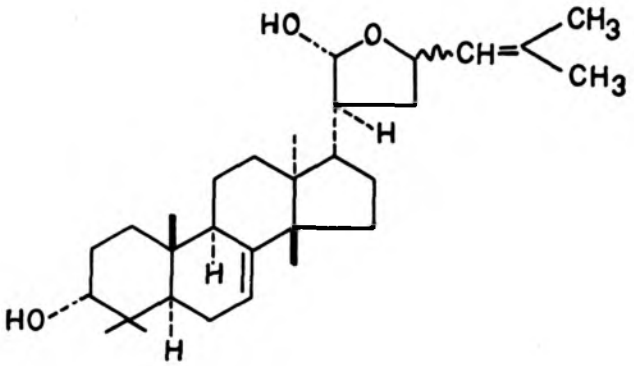
*Veprisone (XXIX) isolated from Vepris bilocularis (Rutaceae) has been shown[69] to be methyl epi-iso-obacunoate, a degradation product of obacunone (XXV).

niabin and D ring* in andirobin have suffered an oxidative cleavage. Thus niabin and andirobin are considered as the first C_{26} triterpenoids of the above series to have the C and D ring oxidised and broken respectively. Structural and stereochemical investigations of all the above compounds have further shown that biogenetically they are derivable[30,36,61] from a triterpene precursor of apoeuphol type (XXXI).



XXXI



XXXII

Another interesting triterpene alcohol flindissol ($C_{30}H_{48}O_3$) (XXXII) has been reported by Birch et al.[70]. It has been further suggested by them that biogenetically it may represent an intermediate stage between triterpenes carrying full side chain and those like limonin group

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*Recently, methylangolensate isolated from Entandrophragma species has been shown[33a] to contain a cleaved D ring.

which carry only a furan ring. It is the first compound reported to possess both a potential furan ring and an intact side chain. From its structure (XXXII) it appears that it is closely related sterically and structurally to the limonin group of triterpenes. Further weight is lent to this hypothesis from the fact that Flindersia species from which Flindissol is isolated have been found botanically to be related to Rutaceae and Meliaceae families i.e. another point of great chemotaxonomic interest.

Burseraceae family is considered[7] by many Botanists to be closely related to Meliaceae. Actually Meliaceae differs from Burseraceae in the lack of resin producing ducts, but the other morphological characteristics are the same. The constituents of the species of Burseraceae also may provide a link with those of Meliaceae family. Work in this direction is in progress in this Laboratory.

Mention must be made here about the genus Chloroxylon D.C. the constituents of which have already been discussed. This genus has been included[2,71] by some Botanists in Meliaceae and by some in Rutaceae. Now the work on the constituents of this species by King et al.[42] and Mookerjee et al.[4] throws some light on the above problem. Actually some of the constituents so far studied are the same and some are closely related to the constituents of the

Rutaceaefamily.

This can serve as an excellent example where the confusion due to the complexity of the morphological pattern can be cleared, to some extent, by the isolation of well-defined organic compounds.

It is really a timely advice to the Organic Chemists by Prof. Briggs[72] that while working on natural products they should be always guided by PLANT TAXONOMY.

REFERENCES

1 R.S. Pearson and H.P. Brown, Commercial Timbers of India, Vol.I, p. 334, Govt. of India, Central Publication Branch, Calcutta (1932).

2 S. Krishna and R.L. Badhwar, J. sci. and industr. Res. VIIB, No.10 Suppl. 129 (1948).

3 K.R. Kirtikar and B.D. Basu, Indian Medicinal Plants, Vol.I, p.298, Published by S.N. Basu, Allahabad (1918).

4 E.L. Core, Plant Taxonomy, p.139, Prentice Hall Inc.(1962).

5 G.H.M. Lawrence, Taxonomy of Vascular Plants, p.549, MacMillan Co., New York (1959).

6 E.L. Core, Plant Taxonomy, p.55, Prentice Hall Inc. (1962).

7 Idem., Ibid., p.344

8 N.L. Bor, Manual of Indian Forest Botany, p.255, Oxford University Press (1959).

9 K.R. Kirtikar and B.D. Basu, Indian Medicinal Plants, Vol.I, p.314, Published by S.N.Basu, Allahabad (1918).

10 K.K. Baslas, J. Ind. Chem. Soc., 32, 445 (1955).

11 Idem., Ind. J. Appl. Chem. 22, 122 (1959).

12 K.R. Kirtikar and B.D. Basu, Indian Medicinal Plants, Vol.I, p.314, Published by S.N.Basu, Allahabad (1918).

13 P.R.Ayyar and V.A.Patwardhan, J. Ind. Inst. Sci. 18A, 19 (1935).

14 M. Qudrat-i-Khuda and M. Hosain, Pak. J. Sci. and Ind. Res. 3, 122 (1960).

15 N.C. Deb, Indian Soap Journal 6, 223 (1940).

16 K.R. Kirtikar and B.D. Basu, Indian Medicinal Plants Vol.I,p-80 Published by S.N.Basu, Allahabad (1918).

17 C.R.Watson, N.G. Chatterjee and K.C.Mukerjee, J. Soc. Chem. Ind. London 42, 387T (1923).

18 a) S.Siddiqui, Curr. Sci. 11, 278 (1942).
b) S.Siddiqui and C. Mitra, J. Sci. and Ind. Res. 4, 5(1945)

19 a) C. Mitra, P.N. Rao, S.Bhattacharji and S.Siddiqui, J. Sci. and Ind. Res. 6B, 19 (1947).
b) C. Mitra, and S.Siddiqui, Curr. Sci. 17, 51 (1948).

20 S. Bhattacharjee, C. Mitra and S. Siddiqui, J. sci. and Industr. Res. 12B, 154 (1953).

21 C. Mitra, P.N. Rao and S.Siddiqui, ibid. 12B, 152 (1953).

22 C.J. Dasa Rao and T.R.Seshadri, Proc. Ind. Acad. Sci. 15A, 161 (1942).

23 K.S. Pankajamani and T.R.Seshadri, ibid. 36A, 157 (1952).

24 S. Mukherjee and H.C.Srivastava, J. Am. Chem. Soc., 77, 422 (1955).

25 P. Sengupta, S.N. Choudhari and M.M. Khastagir, Tetrahedron 10, 45 (1960).

26 P.K. Ramachandran and P.C.Dutta, J. Chem. Soc. 4766 (1960).

27 M. Fetizon et. J. Delobelle Tetrahedron letters 9, 16 (1960); Bull. Soc. Chim. Fr., 1900 (1961).

28 D. Nasipuri and D.N. Roy, J. Ind. Chem. Soc. 40, 327 (1963).

29 E. Wenkert, V.I. Stenberg and P. Beak, J. Am. Chem. Soc., 83, 2320 (1961).

30 C.R.Narayanan, R.V.Pachapurkar, S.K.Pradhan, V.R.Shah and N.S.Narasimhan, Ind. J. Chem. 2, 108 (1964).

31 K.R. Kirtikar and B.D. Basu, Indian Medicinal Plants, Vol.I, p.321, Published by S.N.Basu, Allahabad (1918).

32 A.G. Perkin, J. Chem. Soc., 101, 1538 (1912).

33 P.P.Pillai and B.S.Rao, J. Soc. Chem. and Ind. London, 50, 220T (1931).

34 D.B. Parihar and S. Dutt, J. Ind. Chem. Soc. 27, 77 (1950); Indian Soap Journal XV, 1 (1949).

35 K.V. Gopinath, T.R.Govindachari, P.C.Parthasarathy, N. Vishwanatha, D. Arigoni and W.C.Wildman, Proc. Chem. Soc. 446 (1961); also see A. Aghoramurthy, I. Dass, S.K. Mukherjee and M.A. Rao, J. sci. and industr. Res. 21B, 95 (1962).

36 a) I.G. Grant, (Miss) J.A. Hamilton, T.A.Hamour, R. Hodges, S.G. McGeachin, R.A.Raphael, J.M.Robertson and G.A.Sim, Proc. Chem. Soc. 444 (1961).

b) R. Hodges, S.G. McGeachin and R.A.Raphael, J. Chem.Soc. 2515 (1963).

c) I.G. Grant, (Miss) J.A. Hamilton, T.A.Hamour, J.M. Robertson and G.A.Sim, J. Chem. Soc. 2506 (1963).

37 G.R. Nagarajan and T.R.Seshadri, J. sci. and industr.Res. 20B, 615 (1961).

38 R.R. Snolders, Canad. J. Chem. 42, 2836 (1964)

a) G. Chiurdoglu and R.R.Snolders et A. Soquet, Bull. Soc. Chim. Belg. 70, 468 (1961).

39 K.R. Kirtikar and B.D. Basu, Indian Medicinal Plants, Vol.I, P.323, Published by B.N.Basu, Allahabad (1918).

40 S.J.M. Auld, J. Chem. Soc. 95, 934 (1909)

41 (Miss) A. Mookerjee and P.K.Bose, J. Ind. Chem. Soc., 23, 1 (1946).

42 F.E.King, J.R. Housley and T.J. King, J. Chem. Soc., 1392 (1954).

43 Rau and J.L. Simonsen, Indian For. Rec. 9, 97 (1922)

44 R.C.Cambie, J. Chem. Soc., 466 (1959).

45 R.P. Hildebrand and M.D.Sutherland, Aust. J. Chem. 12, 878 (1959).

46 a)J.Gough, V.Powell and M.D.Sutherland, Tet. letters 763 (1961).

b) J.M. Gough and M.D. Sutherland, Aust. J. Chem., 17, 1270 (1964).

47 The Wealth of India, Vol.VI, p.29, C.S.I.R.Department of Scientific Research, New Delhi (1962).

48 H.S. Jois, B.L. Manjunath and Ramaih, J. Mysore Univ. 11B, 171 (1941).

49 A.S.Rao, K.B. Dutt, Sukh Dev and P.C.Guha, J. Ind. Chem. Soc. 29, 604, 620 (1952).

50 S. Krishnappa and Sukh Dev, Unpublished work.

51 K.R.Kirtikar and B.D.Basu, Indian Medicinal Plants, Vol.I, p.310, Published by S.N.Basu, Allahabad (1918).

52 K. Kafuku and C. Hata, J. Chem. Soc. Japan 54, 169 (1933).

53 Amirchand, C. Mitra and S.Siddiqui, J. sci. and industr.Res. 7B, 69 (1948).

54 T. Nakabayashi, J. Pharm. Soc. Japan 72, 717 (1952); C.A. 47, 3304 (1953).

55 Bholanath, J. sci. and industr. Res. 13B, 740 (1954).

56 K.R. Kirtikar and B.D. Basu, Indian Medicinal Plants, Vol.I, p.313, Published by S.N.Basu, Allahabad (1918).

57 F.E.King and J.W.W.Morgan, J. Chem. Soc. 4738 (1960).

58 S.C.Guha Sircar and T. Chakravarty, J. Ind. Chem. Soc., 28, 207 (1951).

59 S. Ghosh, T. Chakrabarty and (Mrs) A. Chatterjee, ibid., 37, 440 (1960).

60 a) J.D.Connolly, R. Henderson, A. McCrindle, K.H. Overton and N.S.Bhacca, Tet. letters, 37, 2593 (1964).

b) A.T.McPhail and G.A.Sim, ibid. 37, 2599 (1964).

61 W.D.Ollis, A.D.Ward and R. Zelnik, ibid. 37, 2607 (1964).

62 H. Erdtman in Chemotaxonomy (Edited by T.Swain) p.91, Academic Press, London and New York (1963).

63 A.J. Birch, ibid. p.141

64 a) H. Erdtman in Progress in Organic Chemistry (edited by J.W.Cook) Vol.I, p.22, Butterworths Scientific Publication, London (1952).

b) H. Erdtman in Chemotaxonomy (Edited by T. Swain) p.96 Academic Press London and New York (1963).

65 G.H.M. Lawrence, Taxonomy of Vascular Plants, p.560, MacMillan Co. (1959).

66 a) D.H.R. Barton, S.K.Pradhan, S. Sternhell and J.F. Templeton, J. Chem. Soc. 255 (1961).

b) D. Arigoni, D.H.R.Barton, E.J.Corey and O. Jeger in collaboration with L. Caglioti, Sukh Dev, P.G. Ferrini, E.R.Glazier, A. Melera, S.K.Pradhan, K. Schaffner, S. Sternhell, J.F.Templeton and S. Tobinaga, Experientia XVI, 41 (1960) and references cited therein.

67 A. Akisanya, C.W.L. Bevan, T.G. Halsall, J.W.Powell and D.A.H. Taylor, J. Chem. Soc., 3705 (1961).

68 C.W.L. Bevan, T.G.Halsall, M.N. Hwaji and D.A.H.Taylor, ibid. 788 (1962).

68a C.W.L. Bevan, J.W. Powell and D.A.H. Taylor, ibid., 981 (1963); C.W.L. Bevan, A.H. Rees and D.A.H. Taylor, ibid., 982 (1963).

69 T.R.Govindachari, B.S.Joshi and V.N. Sunderarajan, Tetrahedron 20, 2985 (1964).

69a C.W.L. Bevan, J.W.Powell, D.A.H. Taylor, P. Toft, M. Welford, W.R.Chan, B.S.Hootoo and T.G. Halsall, Chemistry and Industry, 1757 (1964).

70 a) A.J. Birch, D.J. Collins, S. Mohammad and J.P. Turnbull, J. Chem. Soc. 2762 (1963).

b) A.J. Birch, Perf. and Essent. Oil Rec. 587 (1964).

71 J.R.Price in Chemical Taxonomy (Edited by T. Swain) pp.450-51, Academic Press, London and New York (1963).

72 H. Erdtman, ibid., p.122.

CAPTER II

CHEMICAL EXAMINATION OF WOOD FROM

CEDRELA TOONA

CHEMICAL EXAMINATION OF WOOD FROM CEDRELA TOONA

Of the five species of the genus Cedrela Linn, Cedrela toona is the most commercial timber of India. Cedrela toona[1] (Sanskrit: Nandivriksha, Hindi: Tun) is a large tree attaining a height of about 70-100 ft and a girth of 6-10 ft and is found in the sub-Himalayan tract, Assam, Bengal, Western Ghats and other hills of Deccan peninsula.

The wood[2] is reddish brown in colour and is fairly fragrant. It is somewhat light and is used for preparing cigar boxes, light furniture and pencils. Apart from the above utility it has some medicinal attributes[3] also. The bark has been described as astringent and antiperiodic and is recommended in the case of chronic and infantile dysentery and as an external application in the case of ulcerations. The flowers have been used for the isolation of a dye stuff known as 'Gunari' in Bengal.

EARLY WORK

Perkin[4] in 1912 isolated two colouring matters from the flowers and identified them as nycanthin and quercetin.

Pillai et al.[5] examined the essential oil obtained by the steam distillation of the wood and showed that the oil consisted of copaene (35%), some bicyclic hydrocarbons including cadinene (45%) and sesquiterpene alcohols (13%).

The powdered wood of Cedrela toona was subjected to solvent extraction by Parihar et al.[6] who reported the isolation of a lactone named cedrelone, an essential oil and a colouring matter. Further, the essential oil was shown to consist of two unsaturated tricyclic alcohols 'toonol' ($C_{20}H_{34}O$), 'toonalol'($C_{22}H_{32}O$) and an unsaturated crystalline compound ($C_{16}H_{10}O$, m.p. 168°).

PRESENT WORK

The preliminary work reported by Parihar and Dutt[1,6] indicated Cedrela toona, to be a rich source for terpenoids. The compound cedrelone reported by the above authors as $C_{25}H_{30}O_5$ appeared interesting as, if the molecular formula were correct, it could be a member of the hitherto unknown C_{25}-terpenoids. However soon after we had initiated the work, communications[7,8] describing the structure of cedrelone appeared which necessitated abandoning of any further effort in this direction. However, work on the systematic study of the various constituents of the wood especially terpenoids, was continued and the present Chapter describes the results of such an investigation.

For the above study two specimens of wood were collected, one from North Kanara (South India) and other from Nainital forests (North India). The climatic conditions* of these two regions are markedly different and it was thought of

---

*

	North Kanara	Nainital forests
Altitude ..	1500 ft	3000 ft.
Temp. range.	20-30°	5 - 30°
Average rainfall	30-40"	40-60"

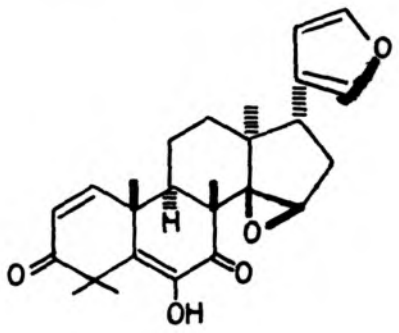
interest to see the variations, if any, in the constituents.

Timber of Cedrela toona of South Indian Origin.

The separation procedure followed for the isolation of various components of the wood is summarised in Fig.1, and Fig.2 gives the thin-layer chromatogram of the various extracts, while Fig.3 shows the various components isolated from the main extract (petroleum ether extract of the extractables obtained after extraction with acetone) and their identification and separation is described below.

Pet. Ether Extract (initial).

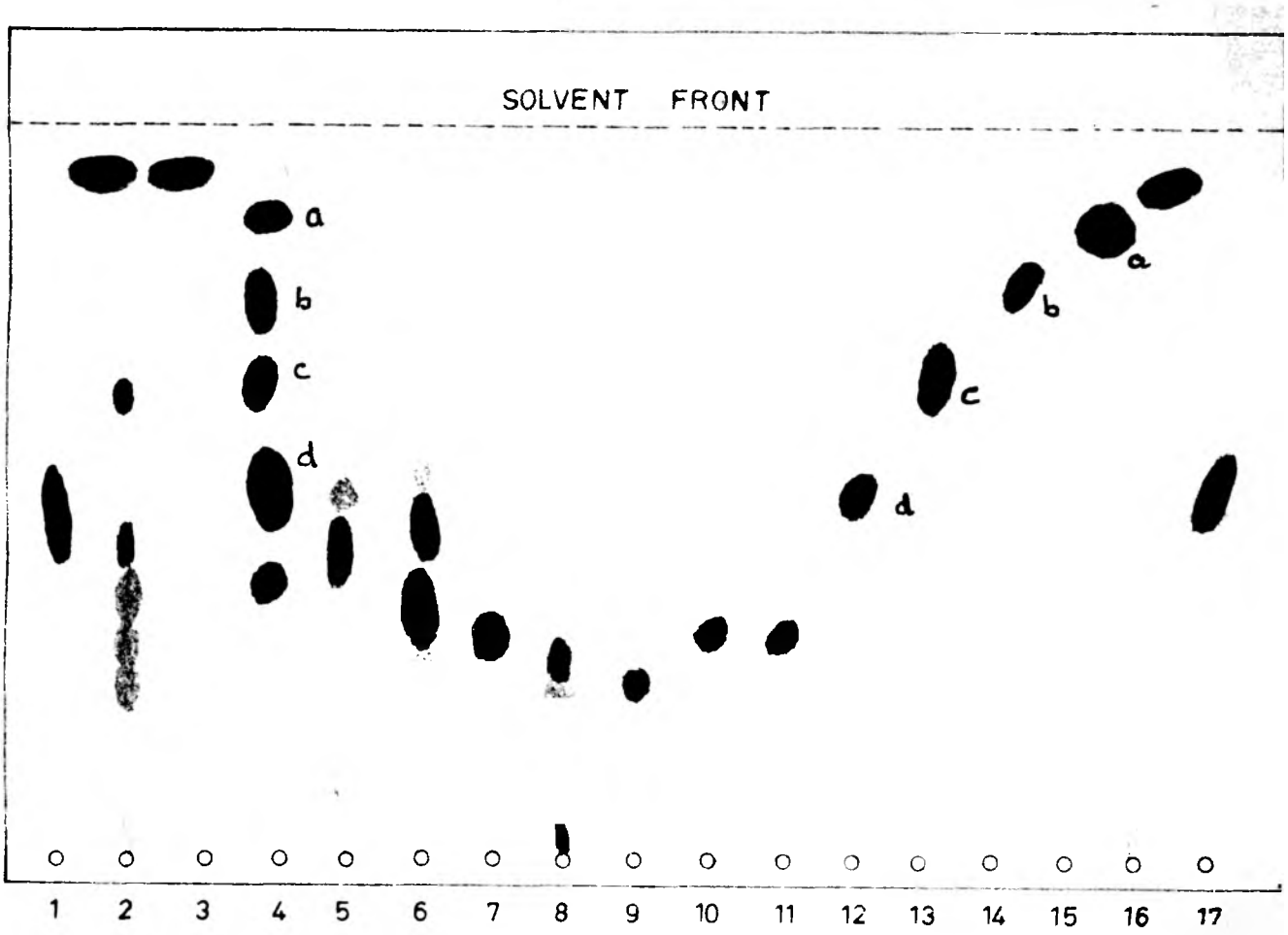
As shown in Fig.1 the pet. ether extract on cooling deposited a solid which was readily identified as cedrelone[7,8] (I). The benzene extract on concentration and work up as detailed



I

in the experimental yielded the major quantity of cedrelone; the mother-liquors obtained from this showed a TLC pattern identical with that of liquid portion of pet. ether extract (Fig.2) and hence they were mixed and subjected to further chromatography.

PLATE —— Silica gel - G.
SOLVENT SYSTEM - n-Heocane : Acetone (80:20)
SPRAYING AGENT - H_2SO_4 : HNO_3 (1:1)

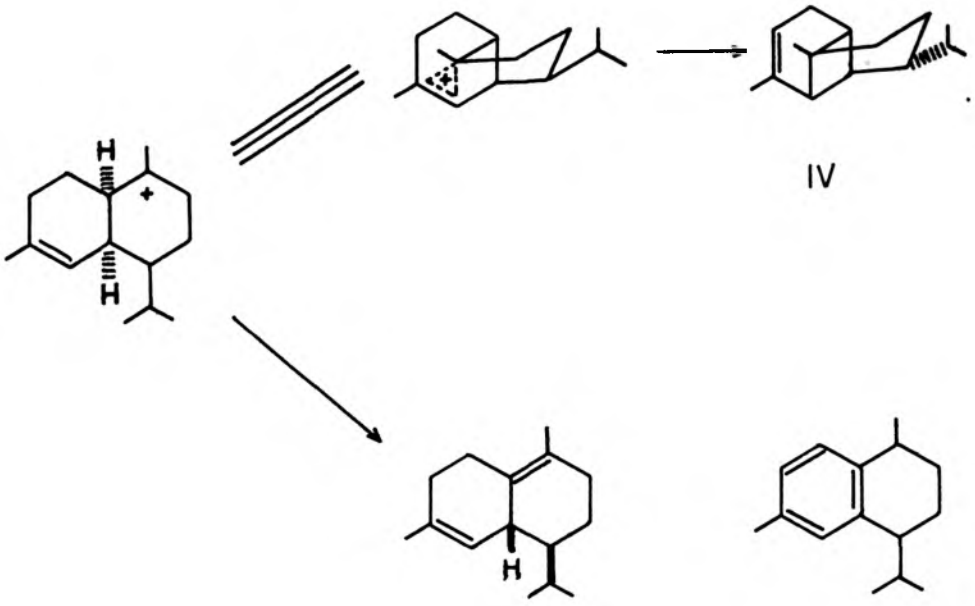


1 & 17) Dye (sudan III) 2) Pet-Ether extract (South Indian) 3) Fraction A'
4) Fraction A'' 5) Fraction B (neutral) 6) Fraction C 7) Fraction D
8) Fraction E 9) Compound X 10) Cedrelone 11) β-Sitosterol 12) Alcohol III
13) Alcohol II 14) Alcohol I 15) Cadelene 16) Pet-ether extract (North Indian

FIG 3. THIN-LAYER CHROMOTOGRAM OF THE COMPONENTS OF CEDRELA TOONA

Fraction A' (copaene, farnesene, δ-cadinene and calamenene):

The lower-boiling fraction (A) was readily separated by chromatography into two fractions viz. Fraction A' and Fraction A". GLC of Fraction A' indicated the presence of atleast 8 components of which three (Fig.4, peak Nos.1,6 and 8) were separated by preparative GLC and identified (vide experimental) as the known sesquiterpene hydrocarbons, copaene, δ-cadinene (III) and calamenene (V). From its retention time, the hydrocarbon corresponding to peak 2 (Fig.4) was identified as farnesene. The structure of copaene has been reinvestigated and forms the subject matter of the next Chapter wherein it has been shown to possess the structure (IV). It may be of some biogenetic significance that δ-cadinene and copaene can be considered to originate from the common biogenetic precursor (II).

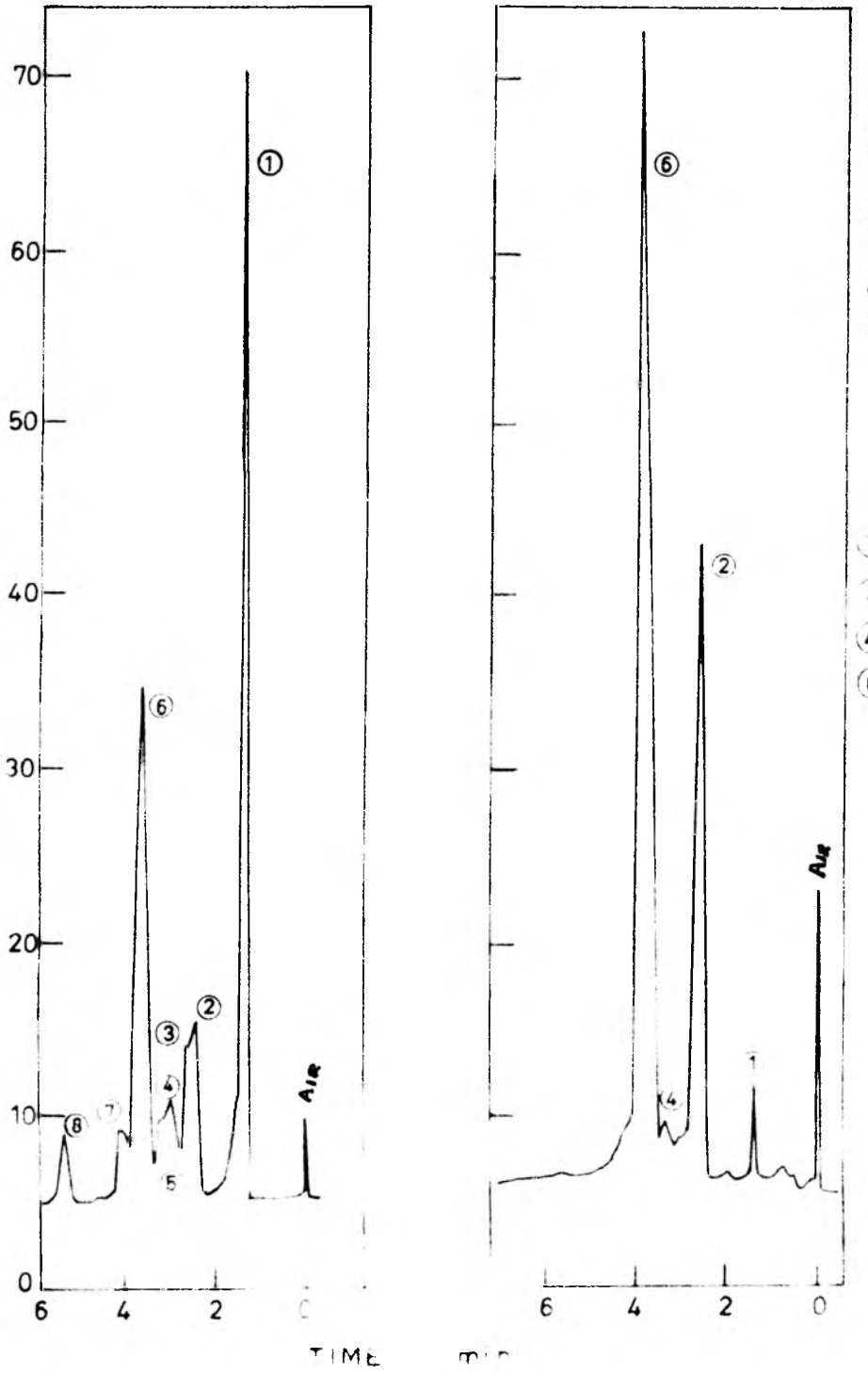


IV

III

V

PERKIN-ELMER VAPOUR PHASE FRACTOMETER, MODEL 154 D



COLUMN — P
TEMP — 160°
PRESSURE — 15 lbs/sq.
CARRIER GAS — H_2
ATTENUATION — 2
SAMPLE — 3 µl

① 38·8 %
② 9·4 %
③ 5·6 %
④ 7·3 %
⑤ 2·9 %
⑥ 26·9 %
⑦ 5·4 %
⑧ 3·4 %

① 3 2 %
② 26 4 %
④ 6·4 %
⑥ 64 %

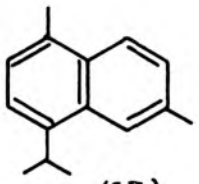
CEDRELA TOONA SOUTH INDIAN CEDRELA TOONA NORTH INDIAN

1) COPAENE 2) FARNESENE 3, 4 & 5 UNIDENTIFIED
6) δ CADINENE 7) UN IDENTIFIED 8) CALAMENENE

FIG. 4. VAPOUR PHASE CHROMATOGRAM OF THE HYDROCARBONS

Fraction A* (some new sesquiterpene alcohols)

Fraction A* by virtue of its method of isolation was expected to represent mostly oxygenated terpenoids. The TLC and GLC of this portion is shown in Fig.3 and Fig.5 respectively and as is clear from these atleast five components appeared to be present. Column chromatography (Al_2O_3/II) yielded besides a small quantity of a hydrocarbon (GLC peak 5 and TLC spot 15) identified (IR and GLC) as cadalene (VI), three new sesquiterpene alcohols (peak No.3 on GLC, and spot Nos.12,13 and 14 on TLC), alcohol I, alcohol II and alcohol III - whereas alcohol III could be readily obtained in a state of purity, the other two alcohols could only be obtained in ~ 90% (GLC) purity. The properties of these compounds have been collected in Table 1.

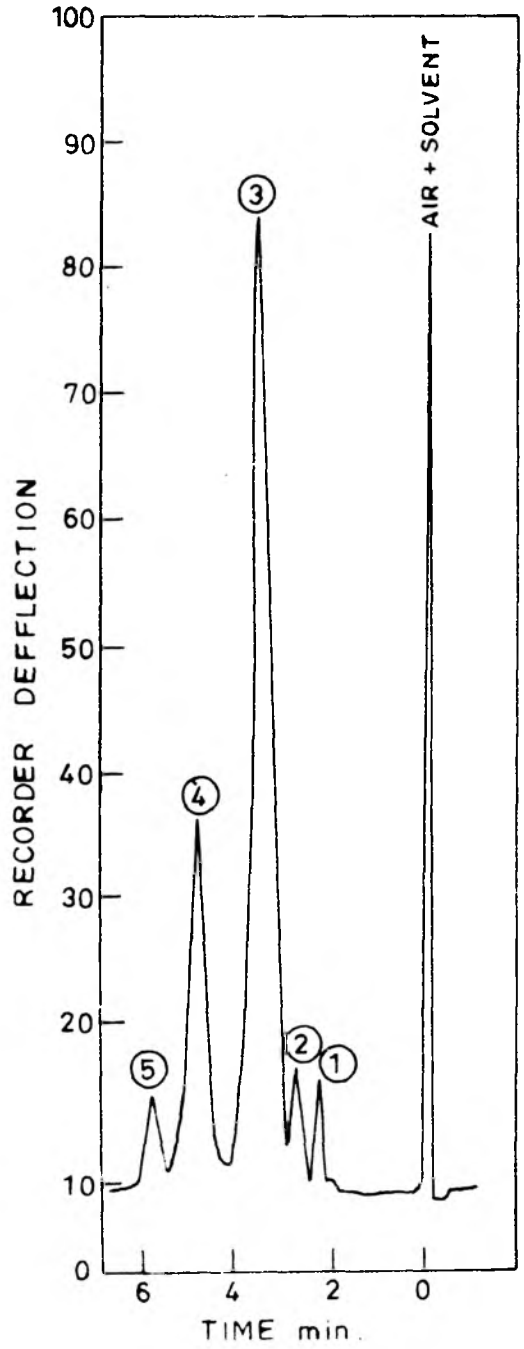


(VI)

TABLE 1. SESQUITERPENE ALCOHOLS FROM CEDRELA TOONA

Compound	%*	Mol. formula	No.of rings	m.p.	b.p./mm	n_D^{30}	$[\alpha]_D^{30}$
Alcohol-I	15	$C_{15}H_{26}O$	bi-cyclic	-	(bath) 160-70/2.5	1.4988	-30.6°
Alcohol-II	31	$C_{15}H_{26}O$	"	-	(bath) 160-80/2.3	1.4998	-100.6°
Alcohol-III	27	$C_{15}H_{26}O$	Tri-cyclic	100-101°	-	-	-11° (26°)

*based on total 'oxygenated' portion.



AEROGRAPH MODEL .
A - 350 - B

COLUMN — P
TEMP. — 180°
CARRIER GAS - H_2
FLOW RATE — 30 ml /min
ATTENUATION - ONE
SAMPLE — 2 ml

① 3·7 %
② 4·4 %
③ 69·7 %
④ 17·8 %
⑤ 4 4 %

1 & 2) UNIDENTIFIED 3) ALCOHOL I, ALCOHOL II AND ALCOHOL
4) UNIDENTIFIED 5) CADALENE

FIG. 5. VAPOUR PHASE CHROMATOGRAM OF FRACTION A"

The IR spectra and the PMR spectra of these compounds are shown in Figs.6-11 and it is clear from these that all the three compounds are tertiary alcohols (absence of any signal assignable to hydrogen attached to carbon carrying oxygen). It may be further concluded from a study of their PMR spectra that alcohol I and alcohol II are closely related and are mono-olefinic and thus should be bicyclic, alcohol III does not show any signal due to a vinylic proton and does not give any colour with tetranitromethane and hence should be tricyclic.

No further work on these have been carried out*.

Fraction B:

In preliminary experiments it was found that this material could not be distilled (even at $\sim 250^{\circ}/0.5$ mm) without extensive decomposition. From its IR spectrum (COOR 1745, 1250; $-(CH_2)_4-$ 735 cm^{-1}) the material was considered to consist essentially of fatty esters. On saponification it yielded a mixture of acids which was not investigated in detail but from the GLC of its methyl esters appeared to consist essentially of the following fatty esters: 1) Palmitate, 2) Oleate and 3) Linolinate.

---

*During the course of this work (structure determination of copaene, Chapter III) it came to our knowledge that Prof. P.de Mayo is also working on the constituents of Cedrela toona. It was mutually agreed that Prof. de Mayo would continue his studies on sesquiterpene alcohols whereas we will restrict ourselves to higher terpenoids.

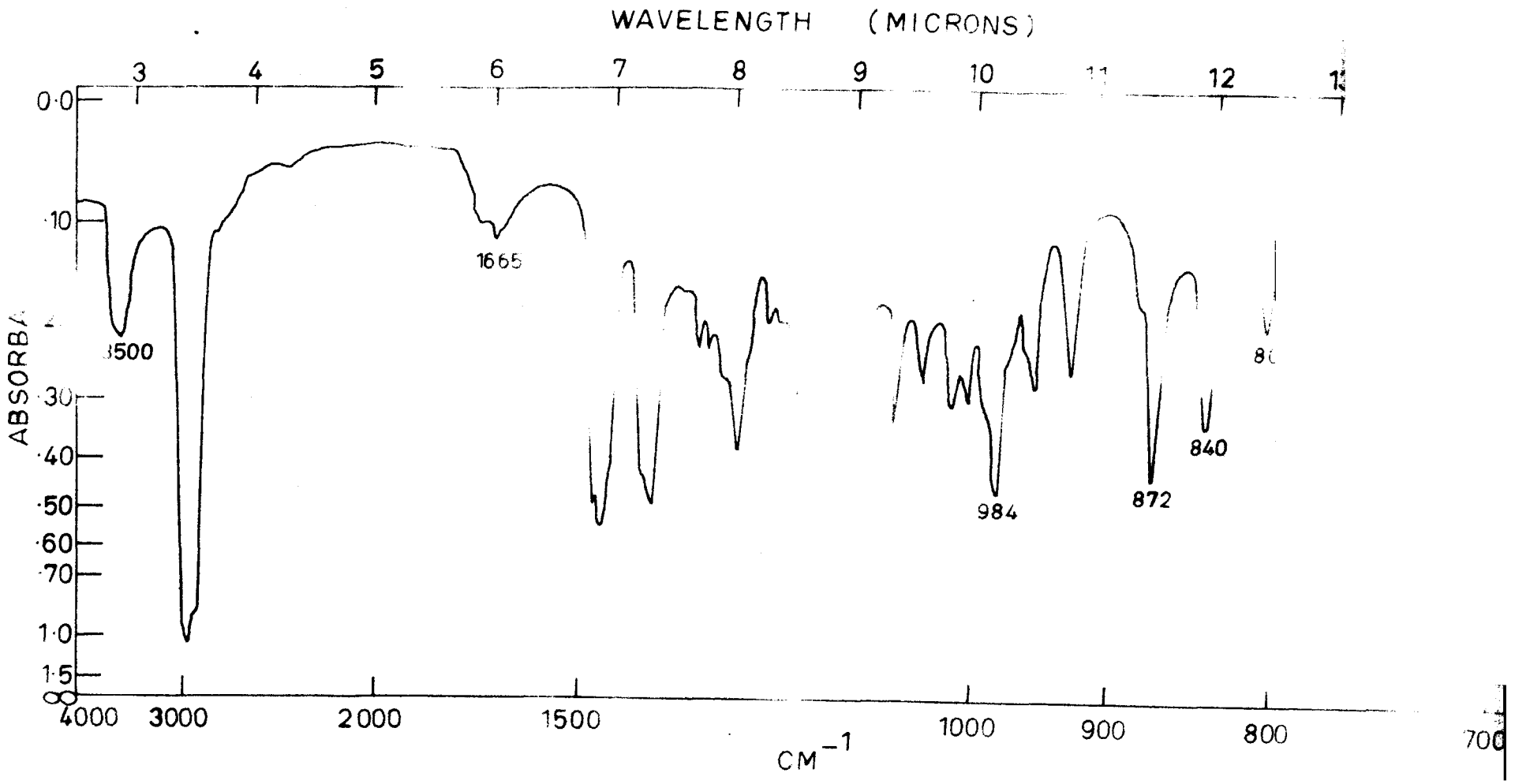


FIG. 6. IR SPECTRUM

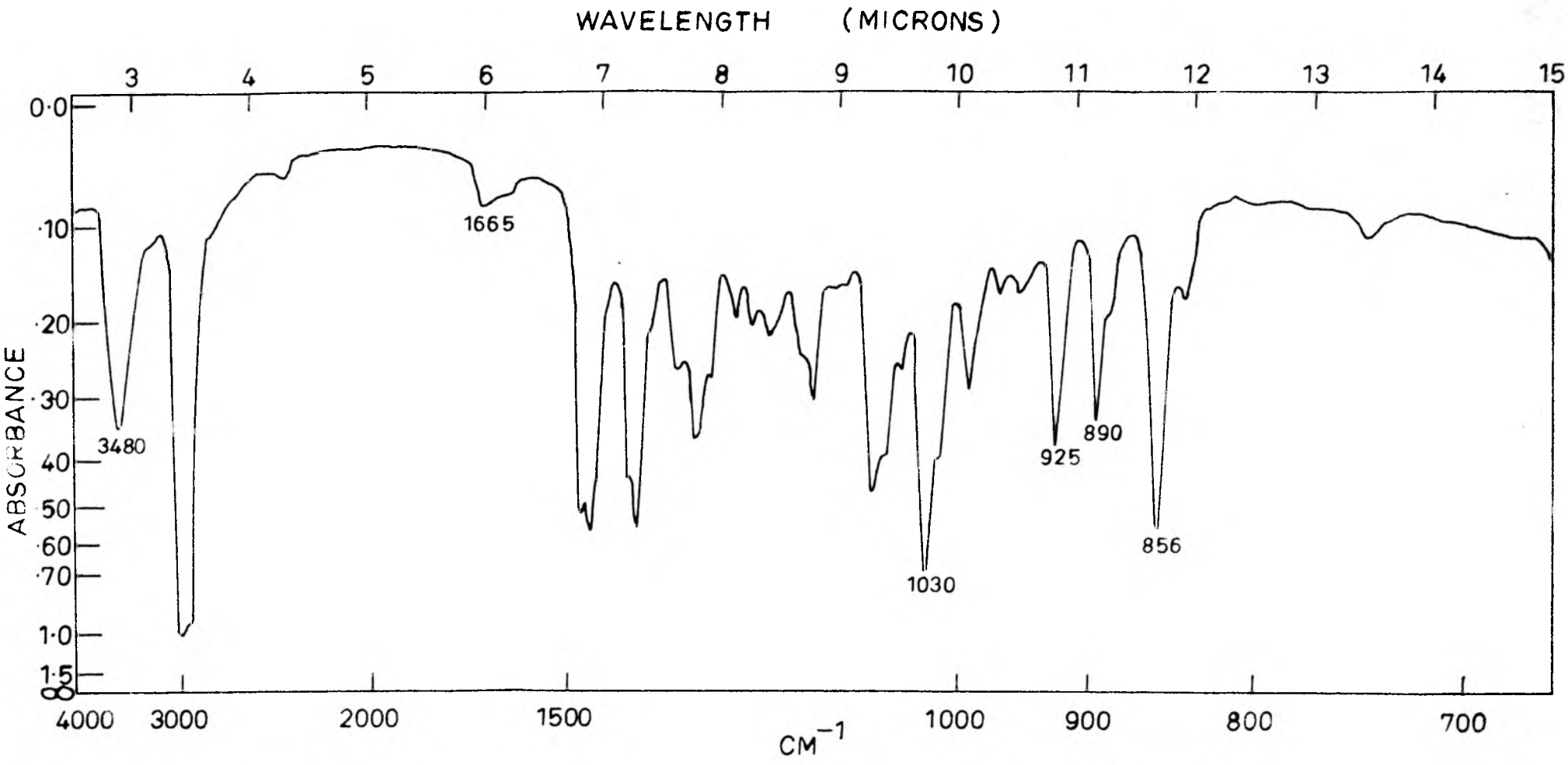


FIG. 7. IR SPECTRUM OF ALCOHOL II

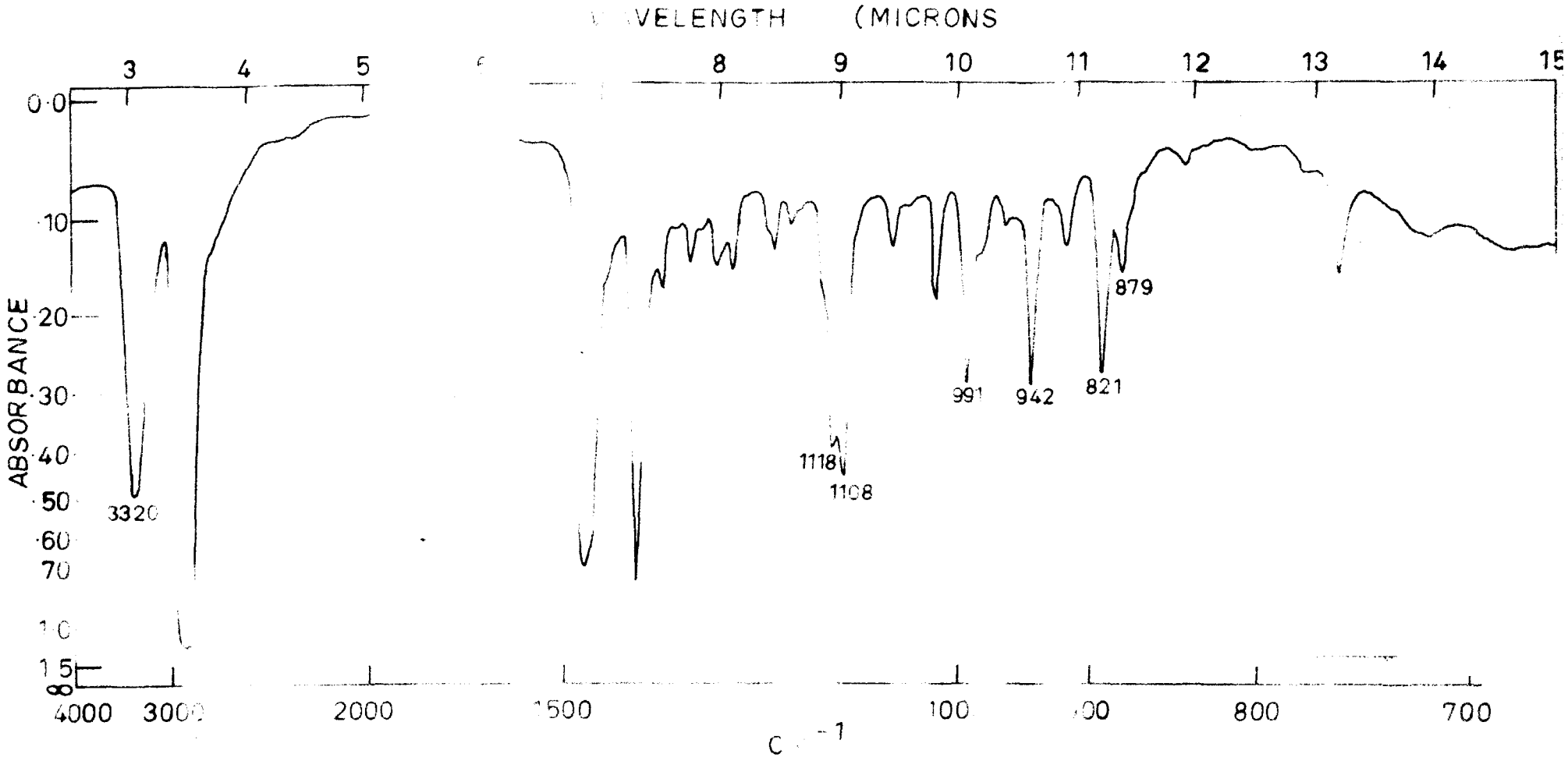

VELENGTH (MICRONS
3
4
5
8
9
10
11
12
13
14
15
0·0
·10
·20
·30
·40
·50
·60
70
1·0
1·5
ABSORBANCE
3320
1118
1108
991
942
821
879
4000
3000
2000
1500
1000
800
700
C - 1

FIG. 8 OF A III

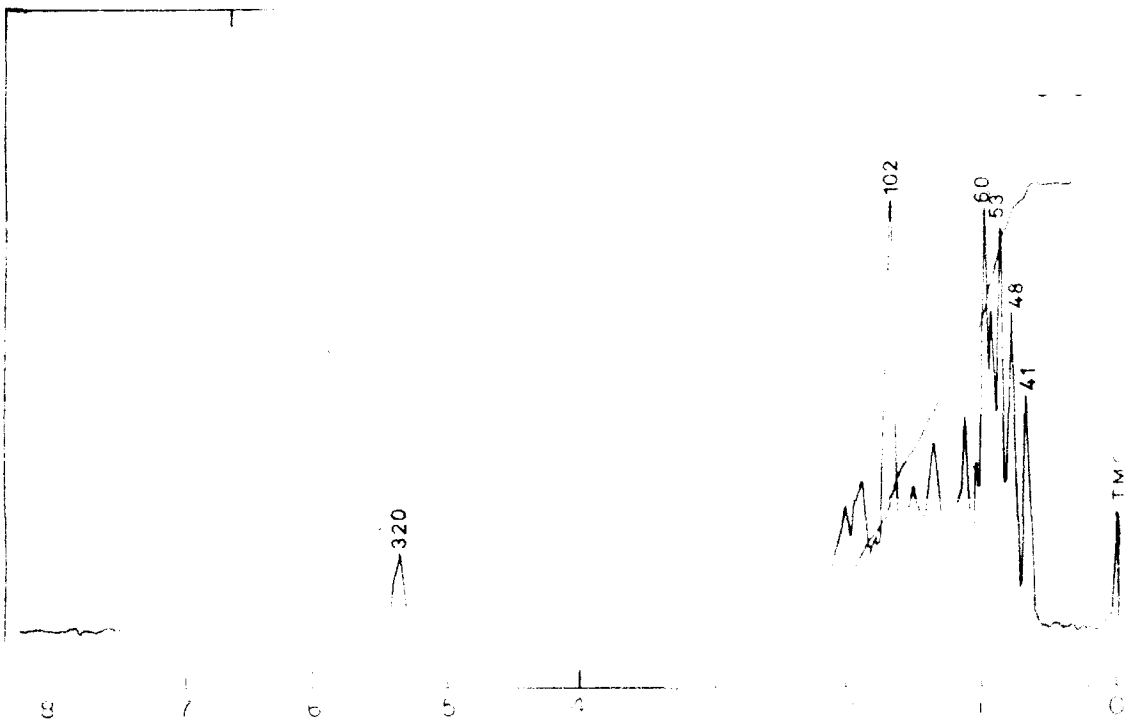


FIG. 9. PMR SPECTRUM OF ALCOHOL – I

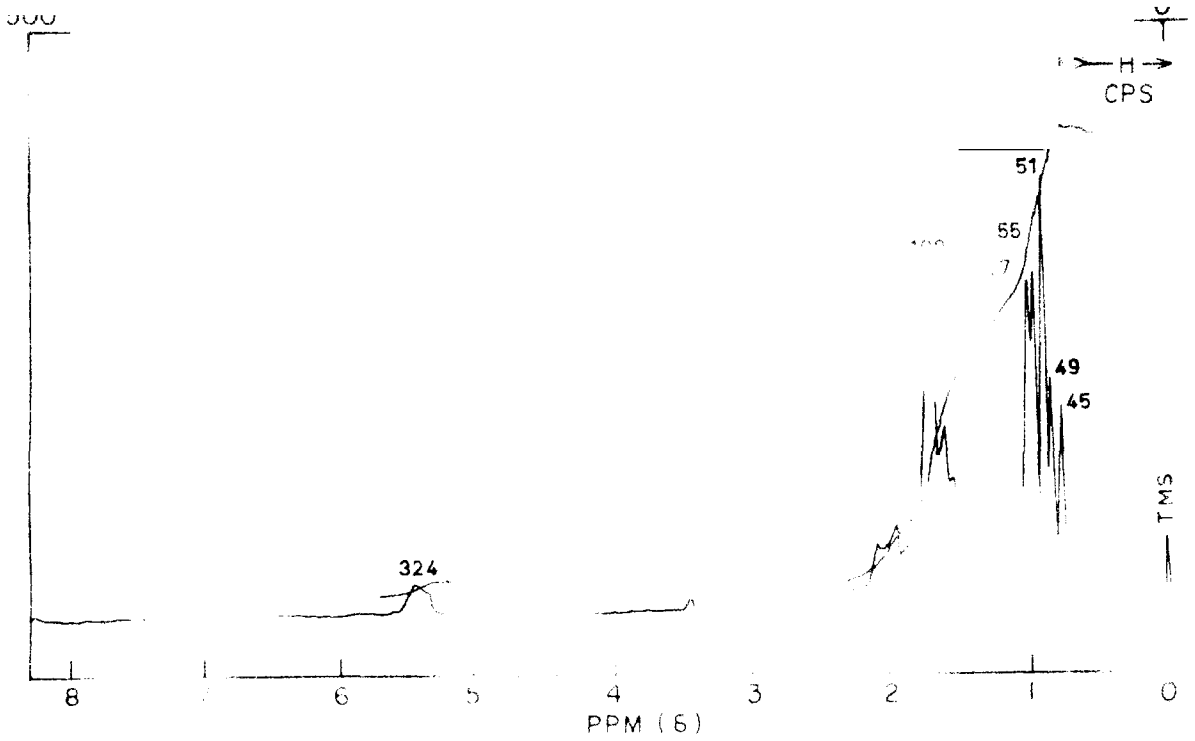


FIG. 10. PMR SPECTRUM OF ALCOHOL

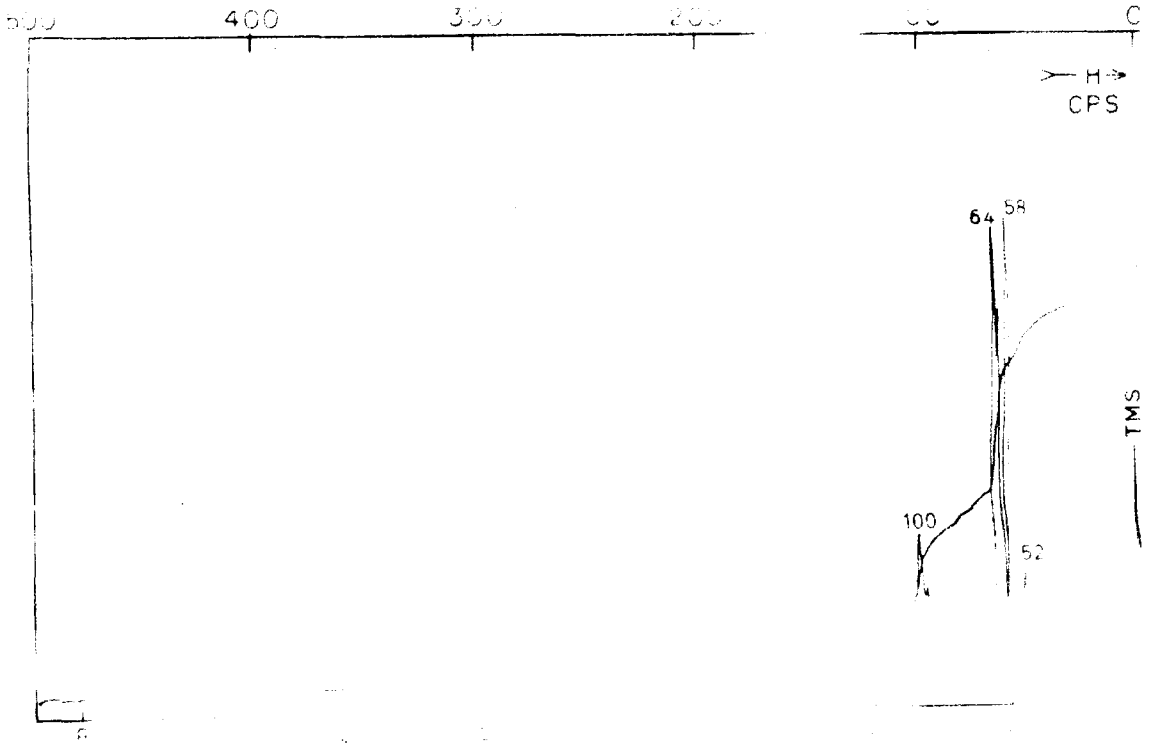
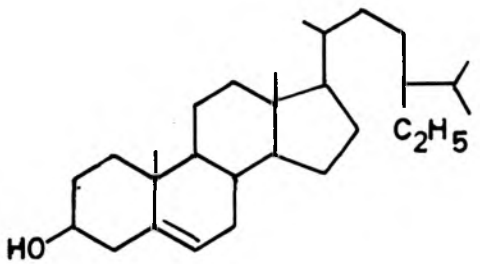


FIG 11 PMR

The neutral portion was shown to consist of β-sitosterol (VII); the presence of alcohol-I, alcohol-II and alcohol-III described earlier was also established; the approximated composition is shown in Fig.1.



VII

Fraction C:

From its TLC this fraction appeared to consist essentially of β-sitosterol and cedrelone. This was confirmed by the actual isolation of these compounds by column chromatography. Presence of compound-X which could be obtained in larger amounts from the North Indian variety of Cedrela toona (vide infra) was clear from the TLC.

Fraction D and E:

Fraction D being available in only small quantity was not studied further, while fraction E as is clear from its TLC (Fig.3) is a complex mixture and no single component could be isolated by its chromatography.

Fraction F:

This portion represents the fatty acids (IR spectrum of methylesters 1745, 1245, 730 cm^{-1}) and we have not examined

in detail. However from the GLC of the methylester its composition has been approximated to be as shown in Fig.1.

Other Extracts: (Ether, Chloroform, Etylacetate, Acetone and Ethanol).

As is shown in Fig.1, the other extracts could be further divided into a benzene soluble and insoluble portions. The soluble portion, as expected, had a composition similar to that of benzene extract (TLC, Fig.2). The insoluble portion showed in the IR bands for OH (3425 cm^{-1}), aromatic nucleus (1615, 1505 cm^{-1}) and from this and its general nature (m.p. above 350°) was suspected to consist of leucoanthocyanins). This appeared to be supported by its colour reaction[9].

The other extracts were not investigated further.

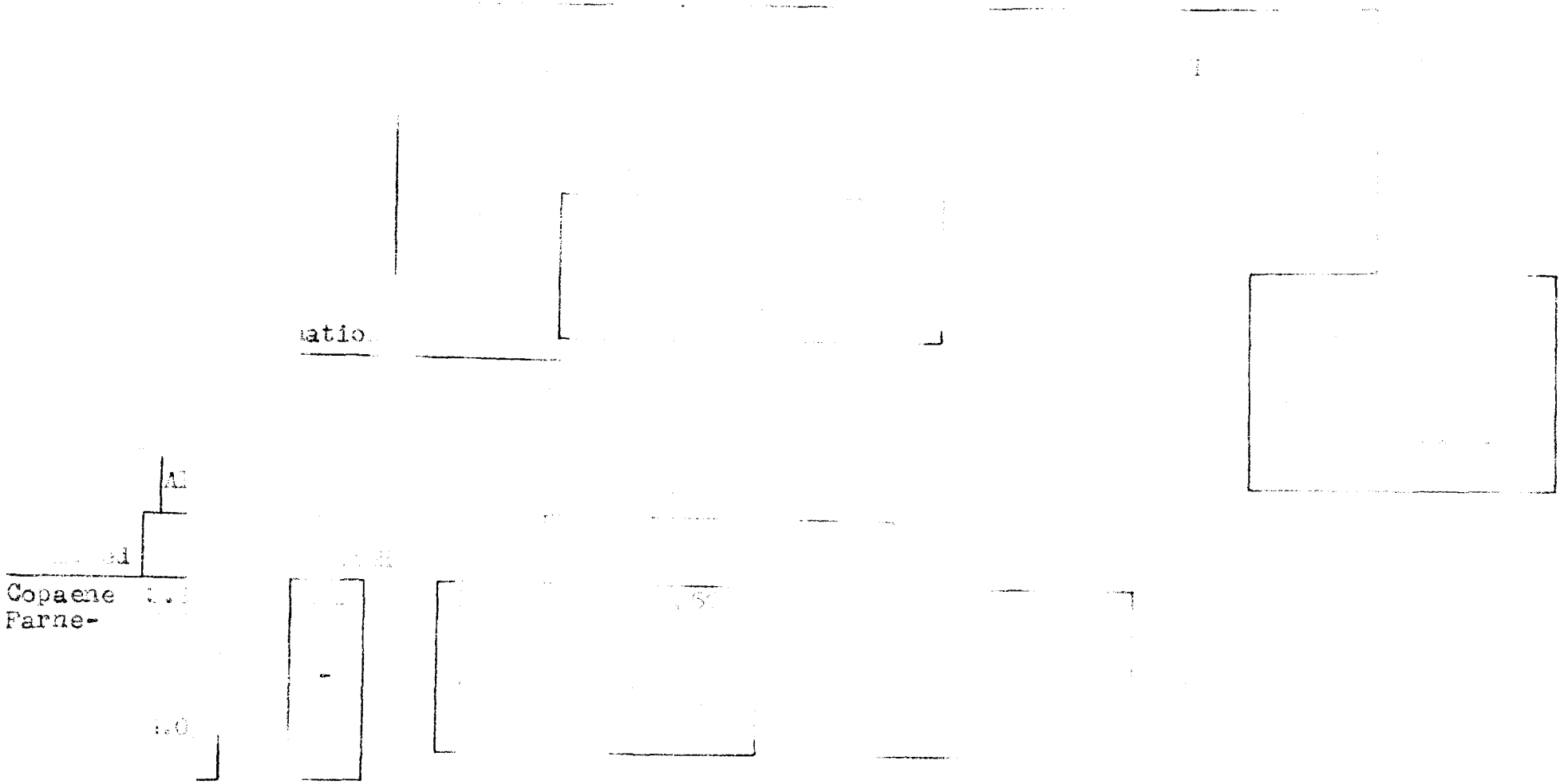
Timber of Cedrela toona of North Indian Origin.

The timber of Cedrela toona (North Indian origin) was subjected to an extraction and separation procedure exactly similar to the one followed for the South Indian variety and depicted in Fig.1. Table 2 shows the comparison of the yields of the various extracts obtained from the two varieties while Fig.2 gives a comparison of the thin-layer chromatogram of the extracts of the two sources. As can be seen, there are significant quantitative differences; as a matter of fact the yield of cedrelone from North Indian variety

LIQUID PORTION (of pet ether extract)

28g

Al_2O_3 nat



was only 3.5% of that from the South Indian variety.

TABLE 2. A COMPARISON OF THE YIELDS OF VARIOUS EXTRACTS FROM CEDRELA TOONA OF DIFFERENT ORIGIN.

No.	Extract	% yield	
		South Indian*	North Indian*
1	Total extractables (acetone)	5.26	9.26
2	Pet. ether	22.5	9.1
3	Benzene	9.9	0.8
4	Ether	12.3	10.23
5	Chloroform	0.3	0.35
6	Ethylacetate	9	12.6
7	Acetone	28	64.75
8	Abs. ethanol.	18	2.27

*Source of South Indian wood .. Shimoga Dist.(North Kanara)

Source of North Indian wood .. Nainital forests (U.P.)
The logs used in this work were of the same girth (girth ~ 1.5', length ~ 3.5').

The pet. ether extract has been subjected to a detailed analysis (Fig.1) following closely the method established for the South Indian variety.

Fraction A:

This was found to consist only of sesquiterpene hydrocarbons. As can be seen from its GLC (Fig.4), its composition is significantly different from that of the

South Indian variety and Table 3 gives a comparison of the two.

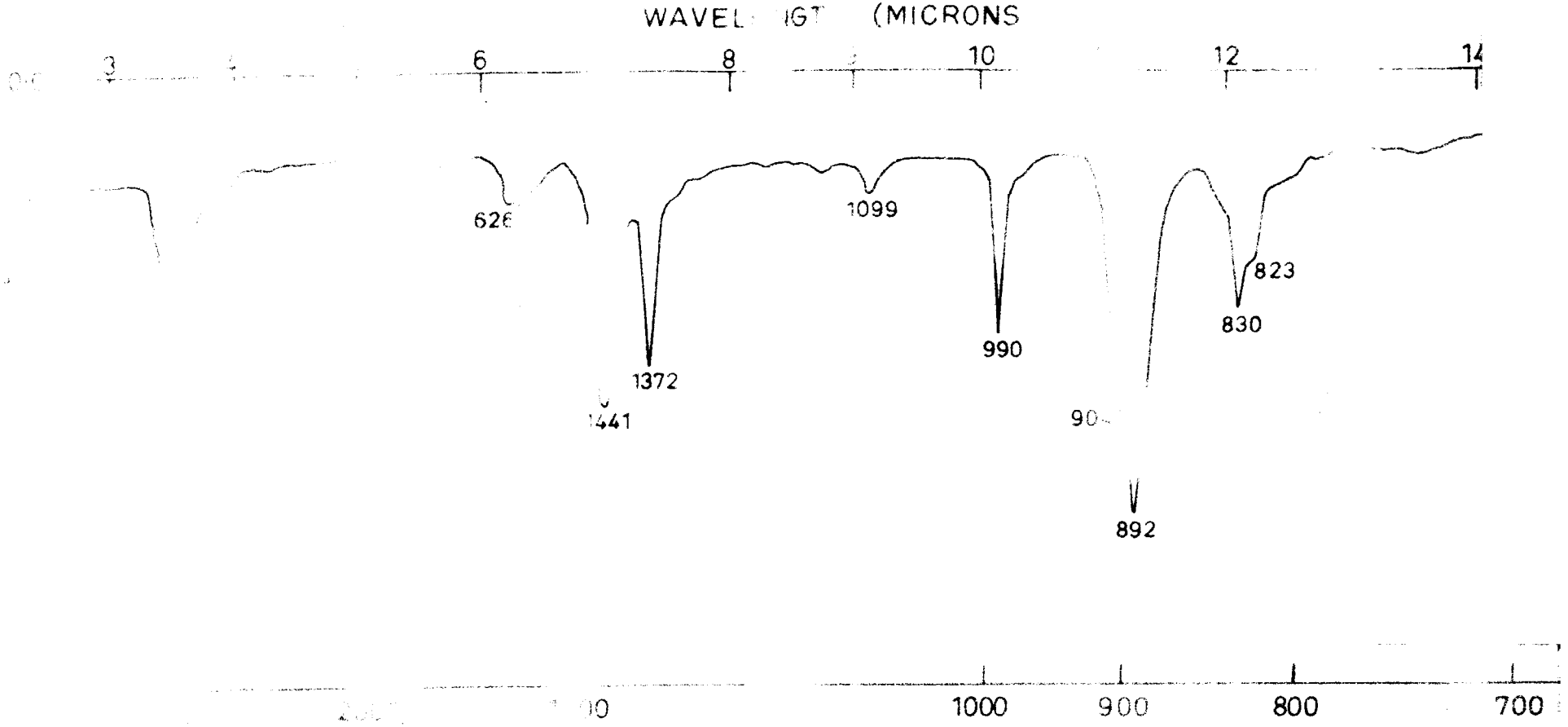
TABLE 3. A COMPARISON OF THE YIELD OF THE HYDROCARBONS FROM CEDRELA TOONA OF DIFFERENT ORIGIN.

GLC peak No.	Compound	% South Indian	% North Indian
1	Copaene	38.8	3.2
2	Farnesene	9.4	26.4
3	Unidentified	5.6	-
4	Unidentified	7.3	-
5	Unidentified	2.9	6.4
6	δ-cadinene	26.9	54
7	Unidentified	5.4	-
8	Calamenene	3.7	-

The major components (peak Nos 2 and 6) have been separated by preparative GLC and while component No.6 was readily identified as δ-cadinene also isolated from South Indian variety. Component No.2 could be obtained pure only from this source. This compound showed $\lambda_{max}^{n\text{-heptane}}$ 225 mμ, ϵ 9772 and from its IR spectrum (Fig.12) was identified as farnesene by comparison with the IR spectrum of an authentic sample.

Fraction B:

This was worked up as described earlier for the other



PECTRUM OF FARN

variety and the component of the neutral and acidic part were checked by TLC (Fig.13) and GLC (Fig.14) respectively. As can be seen, this portion has a similar composition.

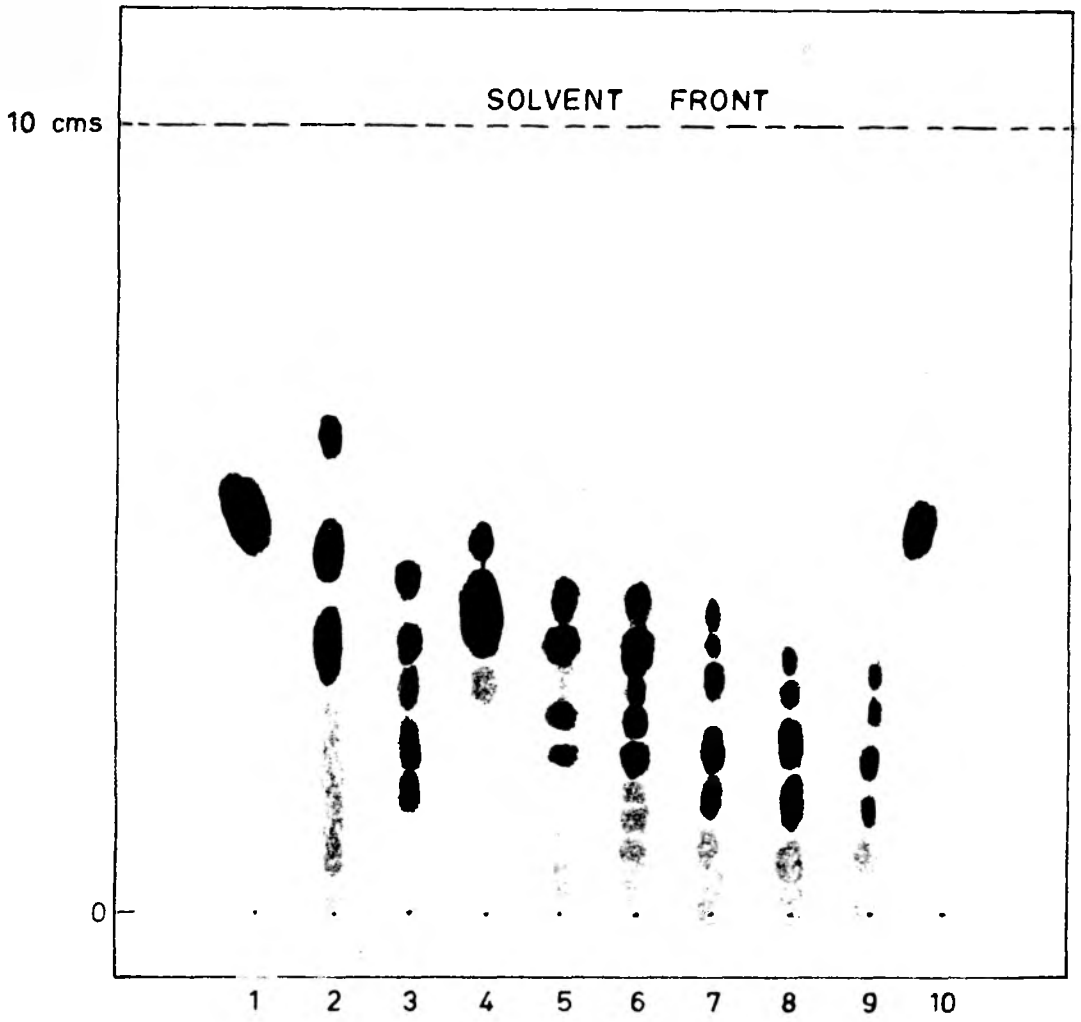
Fraction C:

As can be seen from its TLC (Fig.13) this portion is constituted similarly to the corresponding portion of the South Indian variety. β-sitosterol (VI) cedrelone (I) could be isolated during chromatography and also compound X which could not be obtained pure from the South Indian variety could be obtained in a crystalline state (m.p. 219-24°, $[\alpha]_D^{33}$ -61.5°) from this source. The compound analysed for $C_{28}H_{30}O_4$ and from its NMR (Fig.15) and IR (Fig.16) spectra appears to be closely related to cedrelone and it is planned to study it at a later date.

Fraction D, E and F:

As can be seen from the TLC of D and E (Fig.13) and GLC of the methylesters from F (Fig.14) these portions have a composition similar to ones from the South Indian variety.

PLATE ------ Silica gel G.
SOLVENT SYSTEM -- n-Hexane : Acetone (80 : 20)
SPRAYING AGENT --- H_2SO_4 : HNO_3 (1:1)



1 & 10 Dye (sudan III)

2) Fraction B (South Indian) (neutral)

3) Fraction B (North Indian) (neutral)

4) Fraction C " "

5) Fraction C " "

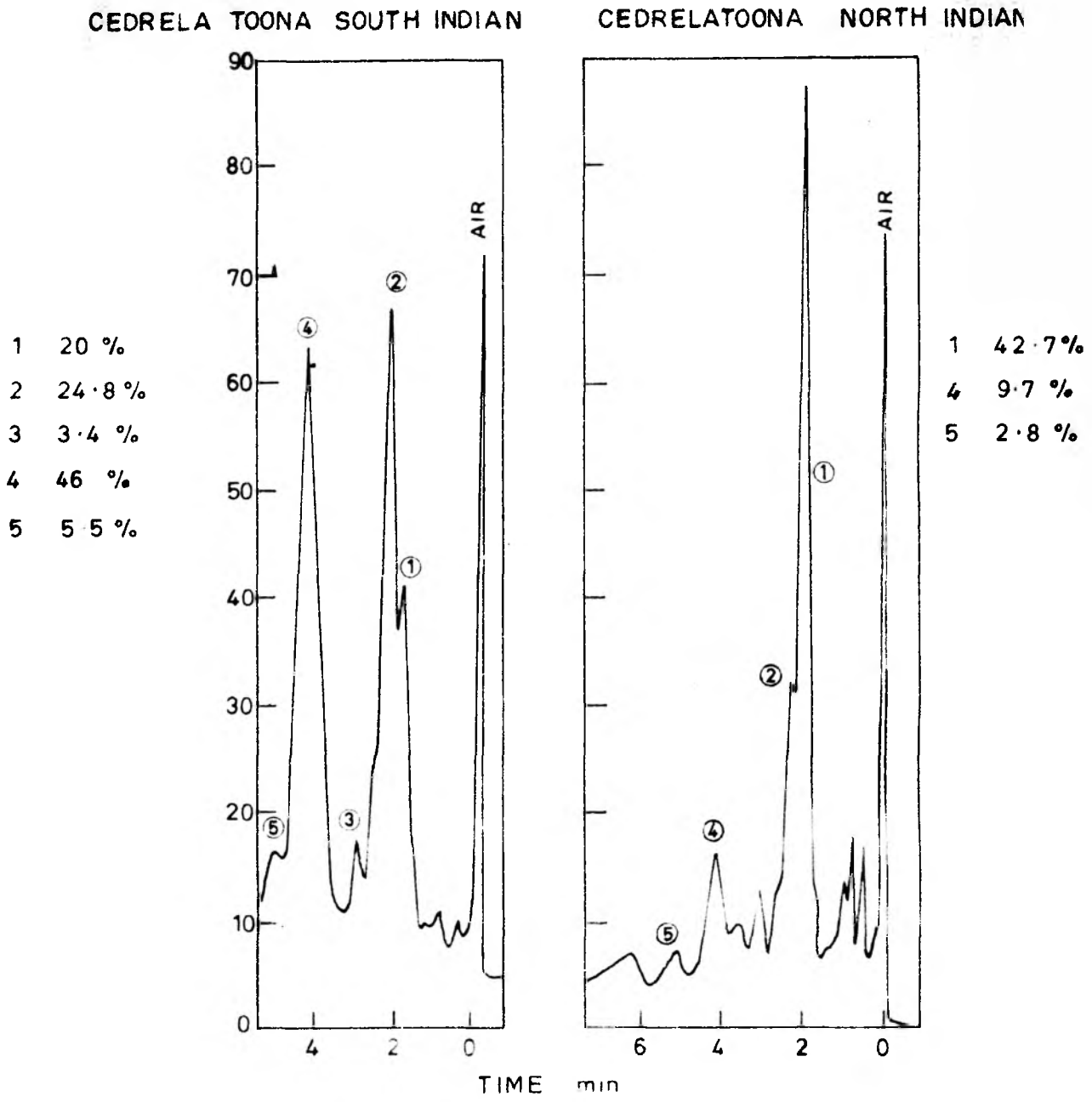
6) " D " "

7) " D " "

8) " E " "

9) " E " "

FIG. 13. THIN-LAYER CHROMATOGRAM OF SOME CONSTITUENTS OF CEDRELA TOONA.



AEROGRAPH MODEL MODEL-A-350 B

COLUMN – P	TEMPERATURE – 180°
CARRIER GAS H_2	FLOW RATE – 70 ml/min
ATTENUATION – ONE	SAMPLE – 2 µl

1) METHYL PALMITATE 2 & 3) UNIDENTIFIED 4) METHYL OLEATE
5) METHYL LINOLINATE

FIG. 14 VAPOUR PHASE CHROMATOGRAM OF THE ACIDIC COMPONENTS OF FRACTION B

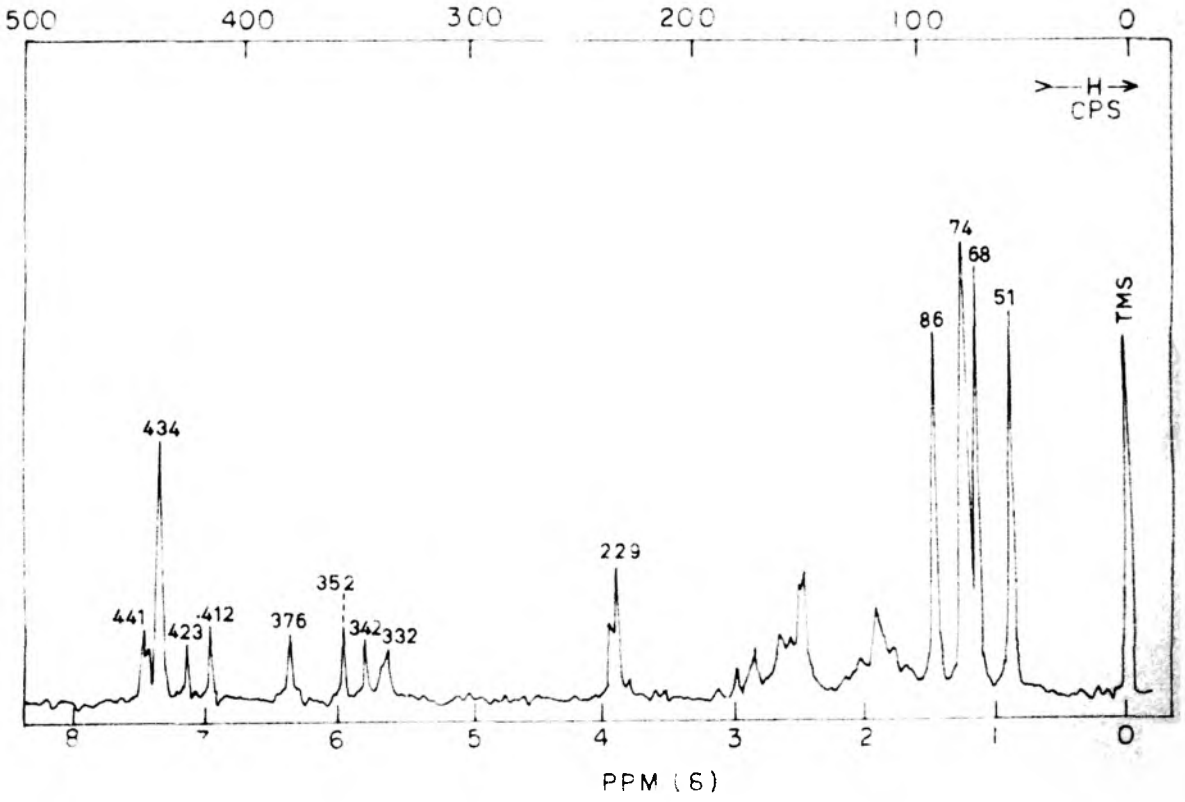


FIG 15. PMR SPECTRUM OF COMPOUND - X

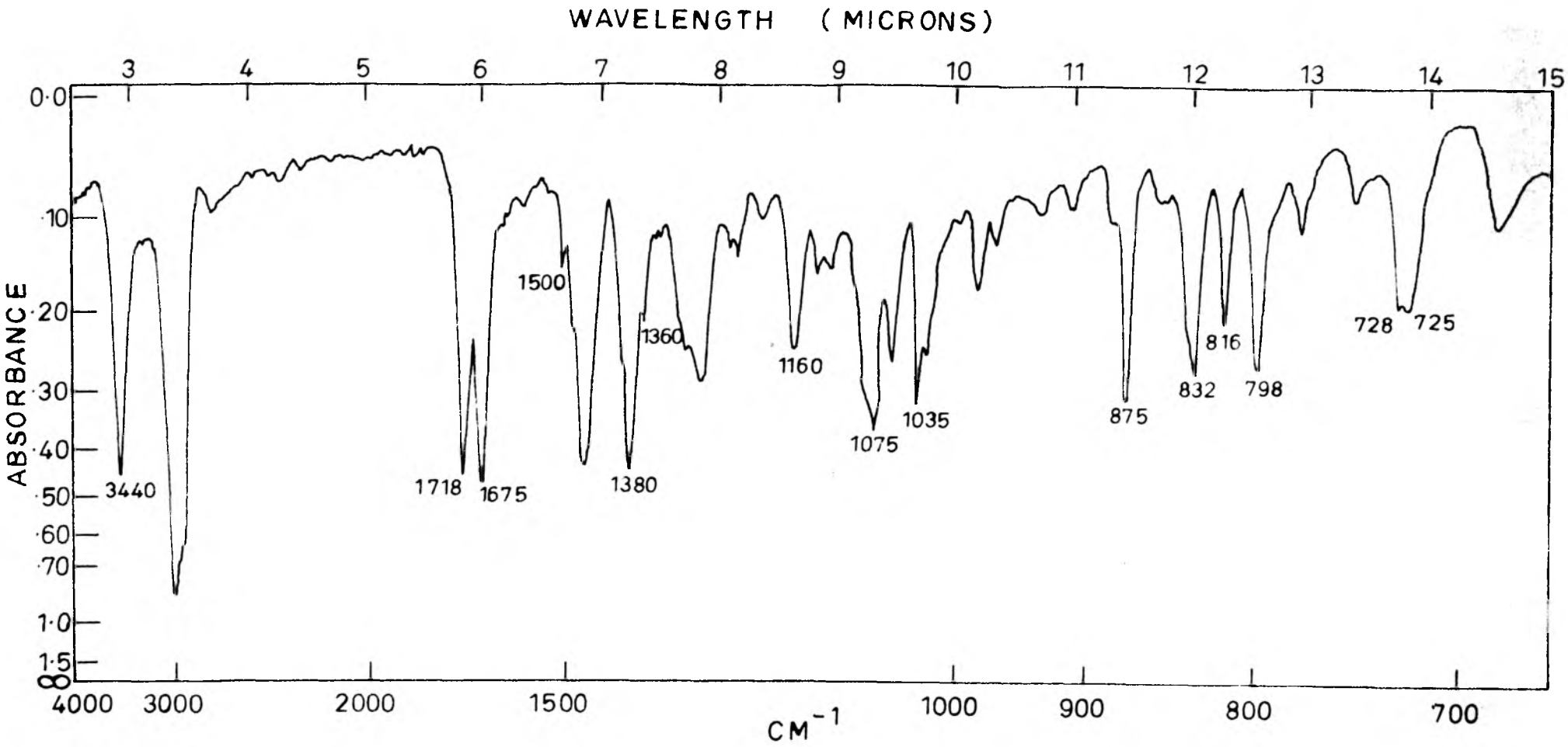


FIG. 16. IR SPECTRUM OF COMPOUND X.

E X P E R I M E N T A L

All m.ps. and b.ps are uncorrected. Pet.ether refers to fraction b.p. 40-60°. Rotations were taken in chloroform, unless stated to the contrary. For tetranitromethane (TNM) tests compound dissolved in minimum quantity of $CHCl_3$ and equal amount of 10% solution of the reagent in $CHCl_3$ were mixed.

UV spectra were measured on a Perkin-Elmer spectrophotometer (Model 350). IR spectra were taken on a Perkin-Elmer Infracord model 137E, either as smears (liquids) or in nujol (solids); maxima are reported in cm^{-1}. All PMR spectra were taken in a ~ 10% solution in CCl_4, unless stated to the contrary, with tetramethylsilane as the internal standard, on a Varian Associates A-60 spectrometer; peaks are reported in c/s from tetramethylsilane peak. GLC analyses were carried out on Perkin-Elmer Vapour Fractometer (Model 154) and on Aerograph (model A-350-B). For preparative GLC the former was used.

Alumina used during this investigation was washed with HNO_3[10] and activated at 450° for 6 hr. The various grades were prepared and standardised according to Brockmann procedure[11]. Thin-layer chromatographies were carried out by using silica gel (mesh 200) containing 15% plaster of paris.

ANALYSIS OF THE WOOD OF CEDRELA TOONA OF SOUTH INDIAN ORIGIN

The wood: The log of wood of Cedrela toona was supplied by the Divisional Forest Officer, Kanara Eastern, Dharwar.

Place of collection: Sirsi range, Shimoga District, North Kanara (South India).

Total acetone extract:

The log of wood (4' x 1-1/4' diameter) was powdered and the powder (19 Kg) was extracted in a soxhlet apparatus in five batches with acetone. The endpoint of the extraction in each batch was determined by the negligible weight of the residue obtained after evaporation to dryness of a test sample (100 ml). All the extracts were combined and the solvent was removed to yield a dark brown semisblid, 1 Kg (5.26% based on the wood powder).

Extraction of the acetone extract with different solvents

The above acetone extract (1 kg) was intimately mixed with celite (1 kg) and the mixture extracted in a suitable soxhlet apparatus successively with pet. ether, benzene, ether chloroform, ethylacetate, acetone and absolute ethanol. The end-point in each extraction was judged as detailed above.

No.	Solvent	Wt (g)	% based on acetone extract.	Remarks.
1	Pet.ether	225	22.5	Dark brown viscous liquid with pleasant odour and some solid precipitated out.
2	Benzene	99	9.9	Brown semisolid.
3	Ether	123	12.3	Buff-coloured amorphous powder, m.p. >350°.
4	Chloroform	3	0.3	Dark brown gummy product.
5	Ethylacetate	90	9	Brick red solid m.p. > 350°.
6	Acetone	280	28	Dark brown shining crystalline solid, m.p. > 350°.
7	Abs. ethanol	180	18	Black shining solid m.p. > 350°.

[For the TLC of all the extracts, see Fig.2]

PET.ETHER EXTRACT

Cedrelone: The solid precipitated in the pet. ether extract was filtered, washed with cold pet. ether to give white rhombic crystals m.p. 185-202°, yield 25 g. It was crystallised twice from benzene:pet. ether (1:1), m.p. 206-208°, yield 18 g. Its m.p. 206-208° suggested it to be cedrelone reported in the literature[7,8] (Lit.[8]: m.p. 209-214°) which was confirmed by its elemental analysis, molecular weight, colour tests and spectral data as described below.

An analytical sample of cedrelone had m.p. 207-208°, $[\alpha]_D^{32}$ -88.6° (c, 0.5%) (Lit.[8]: $[\alpha]_D$ -84.5°). (Found: C, 74.03; H, 7.25. $C_{26}H_{30}O_5$ requires: C, 73.93; H, 7.2%). Molecular weight found by Osmometer method was 427 (calculated 422). It gave dark green colour with alc. $FeCl_3$ and intense red colour with triphenyltetrazolium salt[12]. IR spectrum: 3525, 3100, 1675, 1610, 1505, 1480, 1386, 1380, 1018, 882, 875, 781 cm^{-1}. PMR spectrum: (in ~10% $CDCl_3$ solution): 45, 67, 77, 90, 94 c/s (five tertiary methyl groups), 370, 428 and 441 c/s (3-substituted furan ring), 228 c/s (1H, proton on the epoxide ring), 365 and 414 c/s (2 doublets, J = 10 c/s; vinyl protons), 388 c/s (1H, proton of the disophenol function which disappeared on deuteration).

The liquid portion: The filtrate on concentration weighed, 190 g of which 150 g was chromatographed over Al_2O_3/N (1.5 kg, 30 cm x 8 cm).

Fr.No.	Eluent	Ratio	Volume	Wt(g)	%	Remarks.
I	Pet.ether	-	700ml x 12	83	55	A + B (Fig.1)
II	Benzene	-	700ml x 11	33	23	C (TLC..Fig.3)
III	MeOH:Benz	1:99	700ml x 5	1.5	1	D (TLC..Fig.3)
IV	MeOH:Benz	5:95	700ml x 7	16	11	E (TLC..Fig.3)
V	Refluxed with Na_2CO_3	-	-	15	10	F (Fig.1)

I Pet.ether eluted fraction: Separation of A and B.

The above pet. ether eluted fraction (Fr.I; 83 g) was distilled and a fraction, b.p. 115-40°/2.5 mm was collected which was termed as 'Low boiling fraction' (A), wt. 32 g. IR spectrum: 3322, 2899, 2740, 1725, 1664, 1618, 1458, 1443, 1379, 1362, 1235, 1130, 1116, 1070, 1020, 880, 796 cm^{-1}.

The residue (undistilled) was termed as 'High boiling fraction' (B), wt. 41.5 g. IR spectrum: 3425, 2933, 2865, 1745, 1656, 1587, 1462, 1445, 1379, 1285, 1174, 1075, 890, 785, 736 cm^{-1}.

Fraction A: Separation into A' and A" (hydrocarbons and alcohols)

The low boiling fraction (A; 25 g) was chromatographed over Al_2O_3/I (750 g, 22 cm x 4.5 cm).

Fr.No.	Eluent	Ratio	Volume	Wt.(g)	Remarks.
1	Pet.ether	-	250ml x 15	18.7	A' Sesquiterpene hydrocarbons (GLC Fig.4. TLC Fig.3)
2	Benzene	-	250ml x 5	-	Nil
3	MeOH:C_6H_6	1:99	250ml x 8	-	"
4	MeOH:C_6H_6	3:97	250ml x 13	-	"
5	MeOH:C_6H_6	5:99	250ml x 20	6.17	A" Some sesquiterpene hydrocarbons and alcohols (GLC Fig.5 TLC Fig.3).

Total recovery: 24.87 (95%).

Hydrocarbons A'

The three major hydrocarbons (peak No.1, 6 and 8, in Fig.4) were isolated by preparative GLC by injecting the hydrocarbon mixture A' (7 g) on column P (succinic polyester of diethylene glycol on Chromosorb W, 2.5 cm x 3 meters) at 160° using N_2 (15 lbs/sq.in.) as the carrier gas. Three fractions corresponding to each peak (i.e. peak 1,6 and 8) were collected in separate receivers maintained at -10°.

Copaene: The first fraction (corresponding to peak 1) on distillation gave a colourless mobile liquid, b.p. 87-90°/2.7 mm, n_D^{30} 1.4866, d_4^{30} 0.9141, $[\alpha]_D^{31}$ -9° (c, 10%), M_D 65.09 (calc. $C_{15}H_{24}$ 1 64.43), yield 1.6 g. IR spectrum: 3010, 1660, 1382, 1364, 788 cm^{-1}. From its physical constants the hydrocarbon was suspected to be copaene and was confirmed by comparing its IR spectrum[13] with that of the authentic sample. (Lit.[14]: n_D^{20} 1.4851, d_4^{20} 0.8996, $[\alpha]_D^{20}$ -25.8°). PMR spectrum: 48 and 54 c/s (6H, isopropyl group), 48 c/s (3H, quaternary methyl group), 99 c/s (3H doublet J = 2 c/s; methyl on a trisubstituted double bond) and 309 c/s (1H, vinyl proton). The identification was completed by the preparation of cadinene dihydrochloride from copaene.

Cadinene dihydrochloride from copaene: Copaene (0.534 g) was dissolved in dry ether (8 ml) and dry HCl gas was passed through it at ~ -10° for one hr and left as such (24 hr). The ether

was then replaced by pet. ether and chilled. The crystals obtained were filtered, washed with cold pet. ether and dried, m.p. 109-111°. Yield 0.072 g. It was crystallised from ethylacetate, m.p. 112-15°, $[\alpha]_D$ -40°. Mixed m.p. with an authentic sample of cadinene dihydrochloride (m.p. 117-18°) remained undepressed.

Farnesene: Peak No.2 (GLC Fig.4) was identified as farnesene by its identical retention time with that of authentic specimen obtained from the wood of cedrela toona of North Indian variety.

δ-Cadinene: The second fraction (prep. GLC) (corresponding to peak 6) was distilled to yield a colourless liquid, b.p. 108-109°/2.5 mm, n_D^{30} 1.5065, $[\alpha]_D^{30}$ +10.52°, d_4^{30} 0.9241, M_D 65.6 (calc. 2 ⊨ 66.13). (Found: C, 88.3; H, 11.99. $C_{15}H_{24}$ requires: C, 88.2; H, 11.76%). This was suspected to be δ-cadinene further borne out by the comparison of its IR spectrum[13] with that of the authentic sample which were found to be very identical. (Lit.[15]: n_D^{20} 1.5066, d_4^{20} 0.9175, $[\alpha]_D$ +94°).

Calamenene: The third fraction (corresponding to peak 8) on distillation afforded a colourless oil, b.p. 104-105°/2.5 mm, n_D^{30} 1.5200, d_4^{30} 0.9274, $[\alpha]_D^{30}$ -80°, M_D 66.21 (calc. 3 ⊨ 66.67), yield 0.5 g. (Found: C, 90.14; H, 9.52; $C_{15}H_{22}$ requires: C,89.10; H, 9.52%). Bands 1615, 1500 cm^{-1} in IR spectrum and aromatic proton signals in its PMR spectrum suggested it to be calamenene. This was confirmed by comparing its IR spectrum with that of

the authentic sample when they were found to be superimposable. (Lit.[16]: n_D^{25} 1.5153, $[\alpha]_D$ -80°).

IR spectrum: 2900, 1860, 1750, 1615, 1500, 1480, 1380, 1360, 1320, 1260, 1280, 1040, 1050, 990, 946, 908, 882, 818, 802, 762 cm^{-1}.

PMR spectrum: Two doublets (3H each) centred at 44 and 60 c/s. (J, 7 c/s; Isopropyl group). A doublet centred at 75 c/s (3H; J = 7 c/s; methyl group), 136 c/s (3H; aromatic methyl) 402, 404, 412, 418 (3H, aromatic protons).

Fraction A" (Hydrocarbons and alcohols)

Since the GLC and TLC of this fraction (Fig.5 and Fig.3 respectively) revealed the presence of atleast five components, 1 g of it was chromatographed over Al_2O_3/II (30 g, 14 cm x 2 cm). The course of the separation was followed by TLC and GLC.

Fr.No.	Eluent	Ratio	Vol.	Wt(g)	Remarks*
1	Pet.ether	-	20ml x 1	-	-
2	"	-	20ml x 2	0.019	TLC spot..No.15(a) GLC peak 5 Cadalene.
3	"	-	20ml x 2	0.013	TLC showed mixture
4	"	-	20ml x 6	0.091	TLC spot No.14(b) GLC (90% pure) peak 3. Alcohol I.
5	Benz:pet.ether	25:75	20ml x 2	0.095	TLC showed mixture.
6	"	"	20ml x 3	0.106	TLC spot 13(c) GLC (90% pure) peak 3.Alcohol II.

contd....

Fr.No.	Eluent	Ratio	Vol.	Wt(g)	Remarks*
7	Benz:pet.ether	25:75	20ml x 8	0.189	TLC showed mixtures.
8	"	50:50	20ml x 8	0.121	"
9	Benzene	-	20ml x 9	0.156	TLC spot No. 12(d). GLC (single peak) No.3. Alcohol III.
10	MeOH:Benzene	1:99	20ml x 5	0.019	TLC showed mixtures.
11	MeOH:Benzene	1:99	20ml x 8	0.058	TLC single spot. GLC mixture.
		Recovery ...		0.857 g	86.7%

*For TLC, see Fig.3 and for GLC, Fig.4.

Cadalene: Fraction 2, on distillation yielded a colourless mobile liquid, b.p.(bath) 160-70°/2 mm. The quantity available permitted us to take the IR spectrum only which was found to be superimposable with that of cadalene.

Alcohol I: Fraction 4 was distilled to yield a sweetsmelling viscous liquid, b.p.(bath) 160-80°/2.5 mm, n_D^{30} 1.4988, $[\alpha]_D^{33}$ -30.6° (c, 0.5%), yield 0.070 g. (Found: C, 80.42; H, 11.28. $C_{15}H_{26}O$ requires: C, 81.02; H, 11.79%). IR spectrum: (Fig.6). The PMR spectrum (Fig.9) showed the presence of a vinyl proton (1H singlet, 320 c/s). Hence it must be a bicyclic alcohol. As the above data were not comparable with known bicyclic sesquiterpene alcohols it might be a new sesquiterpene alcohol.

Alcohol II: Fraction 6, on distillation afforded a viscous colourless liquid b.p.(bath) 170-190°/2.5 mm, n_D^{30} 1.4998, $[\alpha]_D^{33}$ -100.6° (c, 0.5%), yield 0.900 g. (Found: C, 80.97; H, 11.58. $C_{15}H_{26}O$ requires: C, 81.02; H, 11.79%). IR spectrum: (Fig.7). Its PMR spectrum (Fig.10) revealed it to be a bicyclic tertiary alcohol. Further from the comparison of the PMR spectra of Alcohol I and Alcohol II it was suspected that they might be double bond isomers.

As in the case of Alcohol I, the data given above were not in agreement with any of the known sesquiterpene alcohols, it might be a new sesquiterpene alcohol.

Alcohol III: Fraction 9 was obtained as a crystalline solid, m.p. 88-94°. It was crystallised once from aceto-nitrile and once from pet. ether, m.p. 100-101°. Final purification was done by its sublimation, m.p. 100-101°. $[\alpha]_D^{26}$ -12° ($CHCl_3$) (c, 6.7%) -4.5° (EtOH). (Found: C, 81.0; H, 11.88. $C_{15}H_{26}O$ requires: C, 81.02; H, 11.79%). It gave a negative TNM test. IR spectrum: (Fig.8). The absence of a signal due to a vinyl proton in its PMR spectrum (Fig.11) supported by the negative TNM test led us to believe it to be a tricyclic alcohol. Further, the comparison of the above physical data with the known tricyclic sesquiterpene alcohols revealed it to be a new alcohol.

High boiling fraction B

Saponification: Separation into neutral and acidic fractions

Neutral fraction: The above fraction (B, 2.5 g) was refluxed with ethanolic NaOH (5%, 5 g NaOH) for 10 hr on a waterbath. The alcohol was then distilled off, the product evaporated to dryness, mixed with anhydrous Na_2SO_4 and the mixture extracted in a suitable soxhlet apparatus with benzene for 8 hr. The benzene extract was cooled, washed with water (20 ml x 5), brine (10 ml x 2) and dried over anhydrous Na_2SO_4. The solvent was completely removed to yield the neutral portion as a gummy product, yield 1.69 g. TLC (spot No.5, Fig.3) revealed it to be consisting of 8 components whose separation was attempted by chromatographing 1 g of the above fraction over Al_2O_3/II (30.0 g, 15 cm x 2.5 cm) monitoring the separation by TLC.

Fr.No.	Eluent	Ratio	Volume	Wt(g)	Remarks*
1	Pet.ether	-	20 ml x 1	-	-
2	Pet.ether	-	20 ml x 2	0.100	Mixture of hydrocarbons including cadalen
3	Benz:pet.ether	25:75	20 ml x 9	0.034	Mixture of Cadalene, Alcohol I and Alcohol II.
4	Benz:pet.ether	50:50	20 ml x 8	0.032	Mixture of Alcohol I and Alcohol II.

.....contd.

Fr.No.	Eluent	Ratio	Volume	Wt(g)	Remarks*
5	Benzene	-	20ml x 6	0.101	Mixture of Alcohol II and Alcohol III.
6	Benzene	-	20ml x 3	0.061	Mixture of Alcohol III and unidentified compound.
7	Benzene	-	20ml x 19	0.231	Mixture of unidentified compounds.
8	MeOH:C_6H_6	1:99	20ml x 12	0.250	β-sitosterol.

Recovery .. 0.889 g (88.9%).

*as revealed by TLC.

Cadalene and Sesquiterpene alcohols (alcohol I, II and III):

As the percentage of cadalene and the sesquiterpene alcohols in the mixture (Fractions 2-6) was quite little they could not be obtained in a pure form. However by comparing the TLC spots with those of the authentic samples the presence of the above compounds with the approximate percentage was established.

β-sitosterol: Fraction 8 crystallised from acetone into white leaflets, m.p. 137-39°, 0.200 g. TLC spot and the m.p. suggested it to be β-sitosterol, further borne out by its IR spectrum which was superimposable with that of the authentic specimen. Mixed m.p. with that of authentic sample remained undepressed.

Cedrelone and Compound X: Though the presence of these compounds was shown by TLC, because of their low percentage they were not obtained during chromatography.

Acidic fraction: The residue, remained after the extraction with benzene of the saponified fraction, was dissolved in water (200 ml) and acidified with dil HCl (congo red). The liberated oil was extracted with ether (30 ml x 4), the combined extracts were washed with water (30 ml x 2), brine (20 ml x 2) and dried (Na_2SO_4). The solvent was removed and the crude acid (0.71 g) was divided into two equal parts and one part was treated with slight excess of diazomethane. The resulting methyl esters were distilled to yield a pale yellow oil, b.p. 135-62°/0.5 mm, yield 0.180 g. GLC (Fig.14) revealed it to be methylesters of fatty acids, by comparison with the authentic samples and the following methylesters of the fatty acids were identified: 1) Palmitate 20.3%; 2) Oleate 46.0% 3) Linolinate 5.5%.

II Benzene eluted fraction (C).

This fraction showed 5 spots on TLC (Fig.3, spot No.6) and 28.5 g was chromatographed to effect the separation of the constituents, over Al_2O_3/IV (300 g, 20 cm x 4.5 cm) and the course of the separation was followed by TLC.

Fr.No.	Eluent	Ratio	Volume	Wt(g)	Remarks*
1	Pet.ether	-	200ml x 1	-	-
2	Pet. ether	-	200ml x 9	16.8	Mixture of Alcohol III β-sitosterol, cedrelone and unidentified compounds (2).
3	Benz:Pet.ether	25:75	200ml x 10	4.2	Mixture of unidentified compounds (2) β-sitosterol and cedrelone.
4	Benz:Pet.ether	50:50	200ml x 10	4.6	Mostly β-sitosterol.
5	Benz:Pet.ether	75:25	200ml x 5	0.9	Mostly β-sitosterol.
6	Benzene	-	200ml x 13	1.7	Mixture of cedrelone and compound X.

Recovery ... 28.3 g (99.3%).

*as revealed by TLC.

Alcohol III: Though all the individual fractions of Fraction No.2 showed the presence of this alcohol on TLC it could not be isolated in a pure form as it was found in a mixture of large quantity of unidentified compounds, probably some high boiling esters.

β-Sitosterol: Fractions 3,4 and 5 were crystallised separately from ethanol to yield white crystalline solids, m.p. 132-37°, 134-37° and 134-37° respectively. Mixed m.p.

of all three with one another remained undepressed and hence they were combined and crystallised from ethanol, m.p. 136-37°, $[\alpha]_D^{32}$ -30.6°, yield 7.1 g. It gave a positive Liebermann's test. (Found: C, 82.9; H, 12.3. $C_{29}H_{50}O$ requires: C, 83.99; H, 12.15%). These data suggested it to be β-sitosterol supported by the undepressed m.p. on admixture with an authentic sample. However the identification was completed by comparing its IR and PMR spectra with those of the authentic sample when they were found to be superimposable (Lit.[17]: m.p. 140°, $[\alpha]_D$ -36°).

Cedrelone: Fraction 6 on crystallisation from benzene: pet. ether (1:1) yielded white rhombic crystals, m.p. 200-204° yield 0.62 g. It was identified as cedrelone by its mixed m.p. with an authentic sample which remained undepressed.

IV MeOH:C_6H_6 Eluted fraction (Fraction E).

Fraction E (12.7 g) was chromatographed over Al_2O_3/III (240 g, 18 cm x 4 cm) in an attempt to separate the constituents. (For TLC, see Fig.3, spot 7). But all the fractions were found to be mixtures as revealed by TLC and hence no single compound could be isolated.

Fr.No.	Eluent	Ratio	Volume	Wt.(g)	Remarks.
1	Pet. ether	-	150ml x 10	-	-
2	Benzene	-	150ml x 10	5.0	TLC mixture, gummy in nature.
3	MeOH:C_6H_6	1:99	150ml x 11	5.97	TLC mixture, gummy in nature.
4	"	3:97	150ml x 9	1.1	"
5	"	5:95	150ml x 5	0.23	"

Recovery.. 12.30 (96.85%).

V Fraction F : Fatty acids

Since some compound (~15 g) was held on the column after the elution with MeOH:benzene (5:95) (during the main chromatography of the liquid fraction) the alumina used in the chromatography was refluxed for 2 hr on a waterbath with ethanolic Na_2CO_3 (10%, Na_2CO_3 40 g) to recover the material which was suspected to be acidic in nature. It was then filtered hot and washed with ethanol:water (1:1). From the filtrate the alcohol was distilled off and the residue evaporated to dryness. It was dissolved in water (400 ml), acidified with dil HCl (congo red) and extracted with ether (50 ml x 5). The combined ether layers were washed with water (50 ml x 2), brine (30 ml x 2) and dried (Na_2SO_4). The solvent was removed to yield the dark brown viscous liquid, 15.0 g which was treated with diazomethane (from 30 g, nitrosomethyl urea) and the resulting methylesters fractionated.

Fraction	b.p./0.5 mm	Yield (g)
a	112-50	1.3
b	150-62	3.9
c	162-200	3.2

Residue .. 6.6 g.

The IR spectrum of the above combined fractions (a, b and c) showed it to be consisting of methylesters of straight chain fatty acids. IR spectrum: 3350, 2950, 2900, 1735, 1475, 1450, 1370, 1245, 1235, 1175, 730 cm^{-1}. By comparing the retention time of components on GLC of fraction (a) and (b) with those of the authentic samples of methyl-esters of fatty acids the following esters were found to be present: 1) Myristate 2% 2) Palmitate 22% 3) Stearate 3% 4) Oleate 16% 5) Linolinate 42%.

BENZENE EXTRACT

Cedrelone: Benzene extract which was a brown semisolid (90 g) was crystallised thrice from benzene:pet. ether (1:1), m.p. 206-207°. Yield 50 g. It was identified as cedrelone by its mixed m.p. with an authentic sample which remained undepressed.

The mother liquors on concentration (30 g) showed a TLC pattern similar to that of pet. ether extract (TLC, Fig.2, spot 3).

ETHER EXTRACT

Benzene solubles: The ether extract (123 g) was refluxed with benzene (500 ml) with stirring for one hr. On cooling it was filtered and the residue washed with benzene. The filterate was concentrated to give a brown gummy product (30 g) which also showed a TLC pattern similar to that of pet. ether extract (TLC Fig.2, spot 4).

Benzene insolubles: The residue obtained as buff-coloured amorphous powder on drying weighed 93 g, m.p. > 350°. A small quantity (~ 0.2 g) was boiled with 20% aic. HCl when red colour developed indicating the conversion of leuco-anthocynins into anthocyanidins. IR spectrum: 3425, 2941, 1712, 1616, 1517, 1466, 1380, 1200, 1140, 1105, 1047, 980 and 824 cm^{-1}.

CHLOROFORM EXTRACT

This was obtained as a dark brown gummy product, yield 3 g. Its IR spectrum showed the following bands: 3322, 2907, 2817, 1729, 1608, 1645, 1595, 1504, 1458, 1377, 1263, 1163, 1075, 1031, 873 and 803 cm^{-1}.

METHYLACETATE EXTRACT

This was obtained as a crimsoned crystalline solid, m.p. > 350°, yield 30 g. IR spectrum: 3269, 2890, 2809, 1636, 1595, 1504, 1443, 1372, 1282, 1139, 1059, 1053, 872 and 820 cm^{-1}.

ACETONE EXTRACT

This was a dark brown shining solid, m.p. > 350°, yield 280 g. It displayed the following bands in the IR spectrum: 3279, 2899, 2667, 1686, 1665, 1605, 1508, 1439, 1377, 1282, 1111, 1058, 870, 819, 780 and 769 cm^{-1}.

ABSOLUTE ETHANOL EXTRACT

This was obtained as a black solid, m.p. > 350°, yield 180 g. Its IR spectrum could not be taken as it was not miscible with nujol.

ANALYSIS OF THE WOOD OF GMELINA TOMENTOSA OF NORTH INDIAN ORIGIN

The wood: The wood was procured from the Divisional Forest Officer, Haldwani Forest Division, Haldwani, U.P.

1 Place of collection: Toonikhal block of Chakata range in Haldwani Forest Division.

2 Girth of the tree at breast height: 4-1/2'

3 Height of the tree: 55'

4 Age of the tree : 35-40 years.

Total acetone extract:

The log of wood (3' length and 1-1/2' diameter) was disintegrated to the powder form and the powder (13 kg) was extracted with acetone in a suitable soxhlet apparatus in five lots. The extracts were combined and the solvent was

removed to yield a dark brown semisolid, 1.760 kg (0.26% based on the wood powder).

Extraction of the total acetone extract with different solvents:

The above acetone extract (440 g) was mixed intimately with celite (440 g) and the mixture extracted in a Sohxlet apparatus successively with pet. ether, benzene, ether, chloroform, ethylacetate, acetone and absolute ethanol. The end-point in each extraction was determined by the method already detailed.

No.	Solvent	Wt(g)	% based on the acetone extract.	Remarks.
1	Pet. ether	40	9.1	Dark brown liquid with pleasant odour and some solid precipitated out.
2	Benzene	3.5	0.8	Dark brown semisolid.
3	Ether	45	10.23	Buff coloured amorphous powder, m.p. > 350°.
4	Chloroform	1.5	0.36	Dark black gummy product.
5	Ethylacetate	55	12.5	Brick-red solid, m.p. > 350°.
6	Acetone	285	64.75	Dark brown shining solid, m.p. > 350°.
7	Abs. ethanol	10	2.27	Dark black shining solid m.p. > 350°.

[For TLC of all these extracts, see Fig.2]

PET.ETHER EXTRACT

Isolation and identification of constituents:

Cedrelone: The solid separated in the pet. ether extract was filtered, washed with cold pet. ether and the crystals dried, m.p. 196-202°, yield 1.5 g. The undepressed m.p. on admixture with an authentic sample of cedrelone enabled us to identify this compound as cedrelone.

The liquid portion: The mother liquors on concentration afforded a viscous liquid (38.5 g) of which 28.0 g was chromatographed over Al_2O_3/IV (310 g, 22 cm x 4.5 cm).

Fr.No.	Eluent	Ratio	Volume	Wt(g)	%	Remarks
I	Pet. ether	-	300ml x 22	17	60.7	A + B
II	Benzene	-	300ml x 14	6.4	22.9	TLC Spot No. 5 Fig.12
III	MeOH : C_6H_6	1:99	300ml x 8	1.6	5.7	TLC Spot No. 7 Fig.13
IV	MeOH : C_6H_6	5:95	300ml x 4	0.5	1.8	TLC spot No. 9 Fig.13
V	Na_2CO_3 Reflux	10%	-	2.5	8.9	Fatty F acids. Fig 1

Recovery... 28 g (100%).

Pet. ether eluted fraction: Separation of A and B.

The above pet. ether eluted fraction (I, 17 g) was distilled to collect a fraction, b.p. 110-36°/2.7 mm, yield 3.2 g.

It was termed as 'Low boiling fraction A'. IR spectrum: 3272, 2850, 1642, 1613, 1577, 1458, 1435, 1374, 1362, 1230, 986, 900, 890, 873, 833, 797 cm^{-1}.

The undistilled residue left behind was termed 'High boiling fraction'(8). IR spectrum: 3350, 2950, 1745, 1475, 1380, 1255, 1175, 1100, 890, 725 cm^{-1}.

Hydrocarbons A'

From the intensity of the hydroxyl band (3272 cm^{-1}) in the IR spectrum of fraction A, the alcohol fraction seemed to be present in negligible quantity in it. However fraction A (2.7 g) was chromatographed over Al_2O_3/I (80 g, 22 cm x 2.3 cm).

Fr.	Eluent	Volume	Wt(g)	Remarks.
1	Pet. ether	80 ml x 4	2.65	Sesquiterpene hydrocarbons.

Thus, when almost all the compound was eluted with pet. ether only, it was concluded that Fraction A consisted mostly of hydrocarbons. The two major hydrocarbons (peak 6 and 8, Fig.4) were isolated by preparative GLC. The hydrocarbon mixture A' (1.5 g) was injected on column P (succinic polyester of diethylene glycol on Chromosorb W (2.5 cm x 3 meters) at 160° using N_2 (15 lbs/sq. in.) as the carrier gas. Two fractions corresponding to each peak (i.e. 6 and 8) were collected in separate

receivers kept at -10°.

Copaene: By comparing the retention time of the hydrocarbon (peak 1, Fig.4) with that of an authentic sample of copaene the presence of copaene, though in a small percentage (3%) was established.

Farnesene: Fraction 1 (corresponding to peak 2) isolated by preparative GLC yielded on distillation, a colourless mobile liquid, b.p. 92-95°/3.5 mm, n_D^{30} 1.4927. Comparison of its IR spectrum with the spectra of some known sesquiterpene hydrocarbons revealed it to be very identical with farnesene. Further, the identification of this hydrocarbon as farnesene was completed by measuring the ultraviolet spectrum, which data closely agreed with the reported one. $\lambda_{max}^{n\text{-heptane}}$ 230 mμ ε, 112; 225 mμ ε 9972 (Lit.[18]: n_D^{20} 1.4927 λ_{max}^{hexane} 225mμ ε, 16600).

δ-Cadinene: The second fraction (corresponding to peak 6) obtained from preparative GLC was distilled to yield a colourless oil, b.p. 105-107°/3.5 mm, n_D^{20} 1.5089. The retention time indicated it to be δ-cadinene, further confirmed by the IR spectrum which was superimposable with that of the authentic specimen.

High Boiling Fraction B

Saponification: (Separation into Neutral and Acidic fractions).

Neutral fraction: Fraction B (1.5 g) was saponified and worked up as detailed earlier to afford the neutral fraction

as an orange-brown product 1.3 g. A comparison of the thin-layer chromatogram of this fraction with the corresponding fraction from the other variety of cedrela toona already studied showed (Fig.13) that except cadalene and sesquiterpene alcohols it had the same composition as the latter. Thus the presence of β-sitosterol, cedrelone and compound X was established.

Acidic portion: The acidic fraction obtained (0.185 g) after removing the neutral fraction as mentioned above was treated with slight excess of diazomethane and the resulting methylesters were distilled, b.p. (bath) 190-200°/0.5 mm, yield (0.1 g). A comparison of its GLC with that of the corresponding fraction from the other variety of Cedrela toona showed (Fig.14) that they had a similar composition. The following methylesters of the fatty acids were identified by the comparison of the retention time with those of the authentic samples. 1) Palmitate 42% 2) Oleate 9.7% 3) Linolinate 2.8%.

II Benzene eluted fraction (C)

Thin-layer chromatography of this fraction (Fig.13) showed 4 spots and 6.4 g was chromatographed to effect the separation of the constituents, over Al_2O_3/ IV (65 g, 17 cm x 2.5 cm) monitoring the separation by TLC.

Fr.No.	Eluent	Ratio	Volume	Wt(g)	Remarks*
1	Pet. ether	-	40 ml x 1	-	-
2	Pet. ether	-	40 ml x 5	3.8	Mixture of unidentified compounds and β-sitosterol.
3	Benz: pet. ether.	25:75	40 ml x 4	1.2	Mostly β-sitosterol.
4	Benz: pet. ether.	50:50	40 ml x 6	0.8	Mixture of β-sitosterol & cedrelone.
5	Benzene	-	40 ml x 8	0.6	Mixture of cedrelone & compound X

Recovery 6.3 g (98.42%)

*as revealed by TLC

β-sitosterol: Fraction 3 and 4 on crystallisation from acetone gave white needles, m.p. 135-37°, 1.4 g. It was identified as β-sitosterol by the mixed m.p. method.

Compound X: Fraction 5 was crystallised from benzene when white needles were obtained, m.p. 217-22°, yield 0.230 g. It was crystallised twice from benzene and the m.p. rose to 219-24°. $[\alpha]_D^{33}$ -61.5° (c, 0.5%). (Found: C, 76.74; H, 8.05. $C_{26}H_{30}O_4$ requires: C, 76.82; H, 7.44%). It gave a negative $FeCl_3$ test indicating the absence of diosphenol group. IR (Fig.16). PMR spectrum (Fig.15).

Cedrelone: The mother liquors of compound X were concentrated and crystallised twice from C_6H_6:Pet.ether (1:1) to yield white rhombic needles, m.p.202-06°;

it was identified as cedrelone by mixed m.p. method.

Fraction F (Fatty acids)

The fatty acids held on the column of Al_2O_3 (during the main chromatography of liquid portion) were recovered, (2.5 g) by the method already described, converted into methylesters and the methylesters further fractionated.

Fraction	b.p./1.7 mm	Wt.(g)
a	145-60°	0.6
b	160-65°	0.5
	Residue	1.4 g

The retention time of the components of fraction (a) and (b) were compared with those of the corresponding fractions of the other variety and the comparative study permitted us to identify the following esters present in the mixture.
1) Myristate 1% 2) Palmitate 23% 3) Oleate 45%
4) Linolinate 5%.

BENZENE EXTRACT

Cedrelone: Benzene extract (3.5 g) was crystallised twice from benzene:pet. ether (1:1) to give white rhombic crystals m.p. 200-06°, identified as cedrelone by mixed m.p. method.

The mother liquors on concentration (1.5 g) showed a TLC pattern (Fig.13, spot 3) similar to that of pet. ether extract.

ETHER EXTRACT

Benzene solubles: The ether extract (45 g) was refluxed with benzene (250 ml) and worked up as detailed early to afford the benzene soluble fraction as a brown semisolid (8 g) which also showed a TLC pattern (Fig.13, spot 4) similar to that of pet. ether extract.

Benzene insolubles: The residue obtained as a buff coloured amorphous powder on drying weighed 37 g. m.p. > 350°. A small sample (0.1 g) when boiled with methanolic HCl(20%)developed deep red colour. IR spectrum: 3333, 2899, 2667, 1613, 1515, 1471, 1381, 1289, 1149, 1112, 1083, 1033, 1020, 982, 875, 820, 770, 725 cm^{-1}.

CHLOROFORM EXTRACT

This was obtained as a black gummy product. yield 1.5 g. IR spectrum: 3425, 2985, 2899, 2703, 1706, 1613, 1458, 1374, 1259, 1099, 1022, 805, 720 cm^{-1}.

ETHYL ACETATE EXTRACT

Ethyl acetate extract was obtained as a brick red solid m.p. > 350°. Yield 55 g. IR spectrum: 3448, 2950, 2880, 2740, 1698, 1613, 1515, 1449, 1370, 1282, 1143, 1111, 975, 878, 820, 780 and 720 cm^{-1}.

ACETONE EXTRACT

Acetone extract was a dark brown solid m.p. > 350°, yield 285 g. IR spectrum: 3333, 2857, 1613, 1515, 1471, 1379, 1282, 820, 725 cm^{-1}.

ABSOLUTE ETHANOL EXTRACT

This was obtained as a black solid, m.p. > 350°, yield 10 g. IR spectrum: 3333, 2851, 1613, 1515, 1471, 1379, 1282, 723 cm^{-1}.

SUMMARY

Farnesene, copaene, -cadinene and calamenene have been isolated from the wood of Cedrela toona. Three new sesquiterpene alcohols have been found to occur in this wood. Isolation of a compound $C_{28}H_{30}O_4$, closely resembling cedrelone has been described.

REFERENCES

1 The Wealth of India Raw materials Vol.II, p.104, C.S.I.R. Department of Scientific Research, Govt. of India, Delhi (1950).

2 R.S.Pearson and H.P. Brown, Commercial Timbers of India, Vol.I, p.268, Govt. of India Central Publication Branch, Calcutta (1932).

3 K.R. Kirtikar and B.D.Basu, Indian Medicinal Plants p.321, published by L.M.Basu, Allahabad (1918).

4 A.G.Perkin, J. Chem. Soc. 101, 1538 (1912).

5 P.P. Pillai and B.S.Rao, J. Soc. Chem. and Ind., London 50, 220T (1931).

6 a) D.B.Parihar and S. Dutt, Indian Soap Journal XV, 1(1949)
b) Idem. J. Ind. Chem. Soc. 27, 77 (1950).

7 K.V. Gopinath, T.R.Govindachari, P.C.Parthasarathy, N. Vishvanathan, D.Arigoni and W.C.Wildman, Pro.Chem.Soc. 446 (1961).

8 a) I.G. Grant, (Miss) J.A. Hamilton, T.A.Hamour, R. Hodges, S.G. McGeachin, R.A.Raphael, J.M. Robertson and G.A. Sim, Proc. Chem. Soc. 444 (1961).

b) R. Hodges, S.G.McGeachin and R.A.Raphael, J.Chem.Soc., 2515 (1963).

9 a) O. Rosenheim, Biochem. J. 14, 178 (1920).

b) G.M. Robinson and R.Robinson, Ibid. 27, 206 (1933).

10 E. Lederer and M. Lederer, Chromatography, p.24, Elsevier Publishing Co., New York (1957).

11 H. Brockmann and H. Schodder, Ber. 74, 73 (1941).

12 K.H.Overton in Elucidation of Structures by Physical and Chemical Methods (Edited by K.W.Bentley), Part I, p.36. Technique of Organic Chemistry (Edited by A. Weissberger) Vol.XI, Interscience Publishers, New York (1963).

13 J. Pliva, M. Horak, V. Herout and F.Sorm, Terpenespektren Akademie-Verlag, Berlin (1960).

14 F. Vonasek, V. Herout and F.Sorm, Coll. Czech. Chem. Comm. 25, 919 (1960).

15 V. Herout and V. Sykora, Tetrahedron 4, 246 (1958).

16 J. Ranneberg, Acta. Chem. Scs. 15, 721 (1961).

17 C.W. Shoppe, Chemistry of the Steroids, p.63, Butterworths Scientific Publications, London (1958).

18 F. Sorm, J. Plesiva, Z. Arnold and J. Pliva, Coll. Czech. Chem. Comm. 14, 699 (1949).

CHAPTER III

STRUCTURE OF COPAENE

STRUCTURE OF COPAENE*

In connection with the structure determination of a new sesquiterpene ketone named mustakone it became apparent that the currently accepted structure of copaene[1,2] (I), a tricyclic sesquiterpene hydrocarbon, was untenable. The present Chapter deals with the evidence which enabled us to derive the correct absolute stereostructure for copaene. It was the structural relationship of mustakone with copaene that threw some fresh light on the structure of copaene and hence some points pertaining to the chemistry of mustakone merit a discussion here.

Mustakone was isolated from the essential oil of Cyperus rotundus Linn. and it analysed for $C_{15}H_{26}O$. Its spectral properties ($\lambda_{max}^{ethanol}$ 255 mμ, ε = 5700; IR: $\nu^{C=O}$ 1685 cm^{-1} $\nu^{C=C}$ 1628 cm^{-1}) revealed it to be an α-β unsaturated ketone. Catalytic hydrogenation of mustakone resulted in an uptake of one mole of hydrogen to yield a saturated dihydroderivative indicating that mustakone was a tricyclic compound. That the carbonyl

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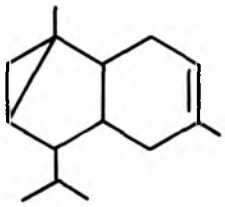
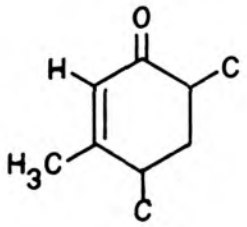
*G. Büchi, J.M. Fearheller, P. de Mayo and R.E. Williams have independently arrived at the same absolute stereostructure for copaene (Proc. Chem. Soc. 214 (1963). Our preliminary note appeared in Tetrahedron Letters 28, 1933 (1963).

function was in a six-membered ring was deduced from the $\nu^{C=O}$ (1712 cm^{-1}) of its dihydroderivative. Further, the ratio of the integrated band intensities of the carbonyl and the C=C stretching vibrations in the infrared spectra of mustakone revealed that carbonyl and the ethylenic functions were in s-trans configuration[3,4].

The proton magnetic spectrum (PMR) of mustakone showed the presence of an isopropyl group (3H signals at 50 and 56 cps), a quaternary methyl group (3H, 58 cps) and a methyl group on a trisubstituted olefinic linkage, (3H doublet centred at 119 cps J = 2 cps; 1H multiplet centred at 335 cps J = 2 cps). From the position of the signal assigned to the vinyl proton it became apparent that the vinyl proton was α to the carbonyl group. Further, mustakone showed no band in the region of 1400-1430 cm^{-1} indicating the absence of methylene groups α to the carbonyl[5,6] or γ to the α-β unsaturated ketone[7]. From all the above data a partial formula (II) could be derived for mustakone. As already stated mustakone displayed its λ_{max} 255 mμ (ε = 5700), but the partial formula now derived, has a calculated λ_{max} 239 mμ[8] and hence some other structural features of mustakone must be responsible for this bathochromic shift.



I



II

In order to find out the nature of the carbon skeleton of mustakone its PMR spectrum was compared with those of a number of known sesquiterpenoids when it was observed that its spectrum was strikingly similar to that of copaene. This suspected relationship was confirmed by the conversion of dihydromustakone to dihydrocopaene by Wolff-Kishner reduction. Thus it became evident that mustakone had the same carbon skeleton as copaene.

The currently accepted structure of copaene is (I)[1,2]. But this structure can neither incorporate the partial formula derived for mustakone nor explain the observed bathochromic shift of mustakone. Thus the structure of copaene became a suspect which prompted us to reinvestigate the problem.

Structure of Copaene

The isolation of copaene was first reported by Schimmel and co.[9] from African copaiba oil. The structural investigations were initiated by Semmler and Stenzel[10] who showed it to be tricyclic and affording cadinene dihydrochloride by the action of hydrochloric acid gas. On the basis of the above data and further degradative work the above authors advanced structure III to it. In view of its relationship with cadinene Henderson et al.[11] modified the structure to IV. Later on, based on the correct structure of cadinene and by the 'labelling method' Briggs and his co-workers[1] fixed the position of the double bond and put forward alternative structures I and V. Out of these two structures, they preferred the structure I, as it would lead to only cadalene on dehydrogenation, as indeed was the experimental fact, while the other structure (V) should lead to cadalene and/or azulene. Since then, the structure I has been in vogue[1,2] though it has been criticised atleast twice. Thus Birch[12] in 1951 was the first to point out that there was no direct evidence for the presence of a cyclopropane ring in copaene and a structure like VI was considered by him as an alternative possibility based on the existing evidence. In his article on the 'Cyclopropane Ring-cleavage in Terpenoids' de Mayo[13] commented that there was no justification for

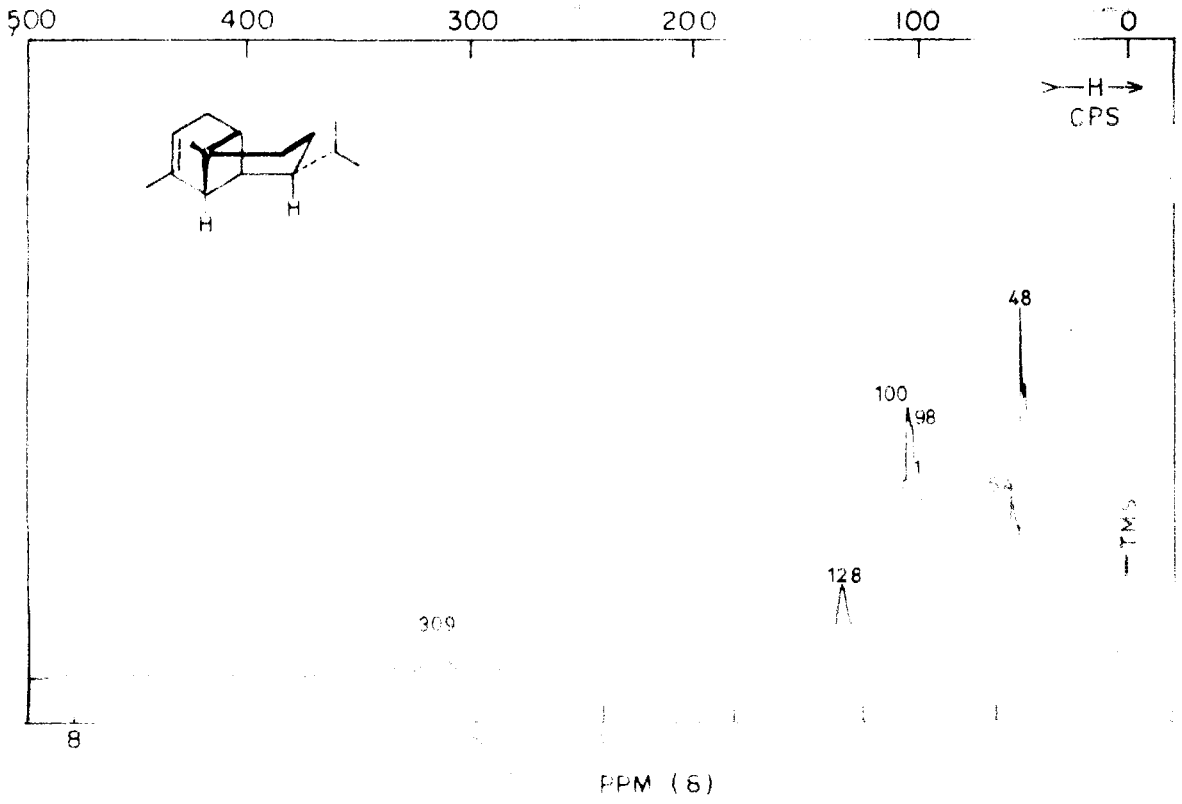


FIG. 1 PMR SPECTRUM OF COPAENE

centred at 33 cps J = 2 cps; 1H unresolved multiplet centred at 309 cps). On the basis of the above PMR data alone all the four structures VI, VII, VIII and IX are readily ruled out. Further, it has already been pointed out that the presently accepted structure of copaene cannot accommodate the structural requirements of mustakone. This made us suspect that copaene may not contain a cyclopropane ring at all, as first pointed out by Birch[12] in 1951. The following observations fully supported this contention.

Catalytic hydrogenation of copaene resulted in an uptake of only one mole of hydrogen and the resulting dihydrocopaene resisted further hydrogenation even under drastic conditions such as in the presence of perchloric acid and at elevated temperature. In contrast to the behaviour of carane which was readily attacked by hydrochloric acid gas, copane was recovered unchanged under these conditions. Refluxing copane with formic acid for four hours resulted in the recovery of the starting material.

Thus the above findings called for a revision of the structure of copaene. An alternative formulation* (XIV),

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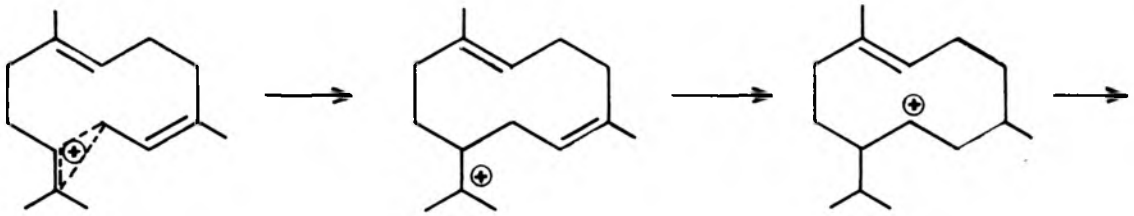
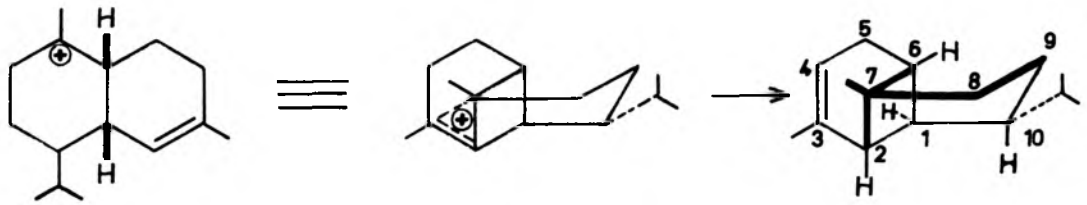
*The genesis of the precursor (XIII) from farnesyl cation has been discussed by de Mayo et al[15] and its role in the biogenesis of the novel sesquiterpenoid helminthosporal established by tracer studies.

derivable as under, looked attractive as it would, not only, explain all the known reactions of copaene but will also provide an expression suitable for mustakone which now becomes XV and is expected to exhibit spectral characteristics similar to those of verbenone[14] (XVI). Moreover this formulation of copaene represents it as a bicyclo [3,1,1] heptane and similar bicyclo compounds are known[15] to exhibit the C-H out-of-plane deformation at lower frequencies due to the strain in the molecule e.g. α-pinene has its δ= CH at 786 cm^{-1}. In accordance with the above behaviour copaene also exhibits its δ= CH at 788 cm^{-1} (Fig.2) which disappears after hydrogenation.



X XI XII



XIII XIV

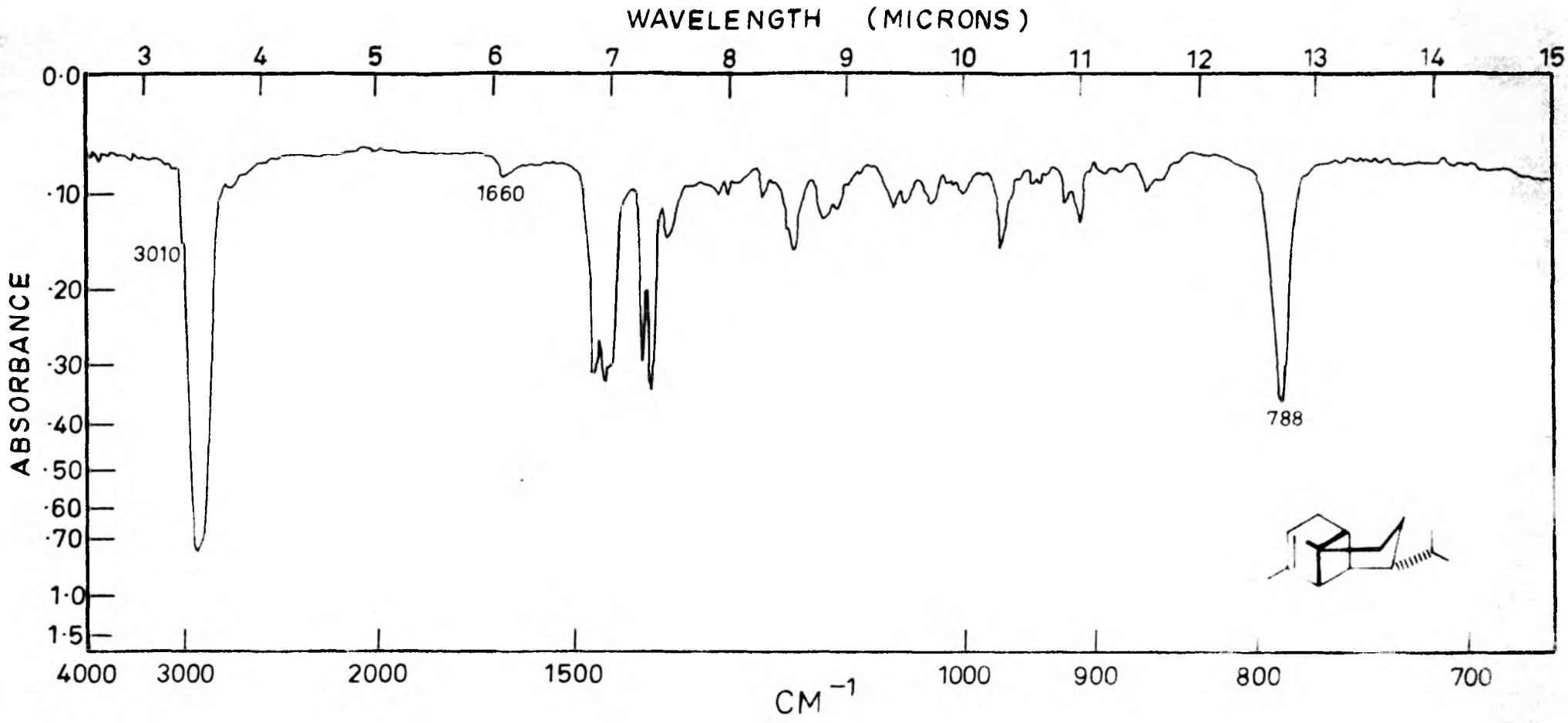
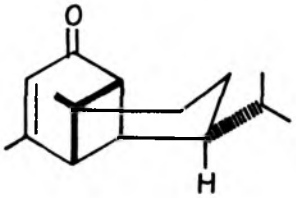


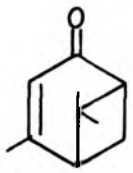
FIG.2 IR SPECTRUM OF COPAENE



XV

λ_{max} 255 mμ

ε 5,700



XVI

λ_{max} 253 mμ

ε 6,840

Decisive chemical evidence in favour of (XIV) was obtained as follows. Ozonolysis followed by the oxidative cleavage of the ozonide with alkaline H_2O_2 yielded the methyl keto acid of Semmler et al. which was characterised as its semicarbazone (m.p. 218.5 - 220°). However, surprisingly, when the oxidative cleavage of the ozonide was carried out using H_2O_2 in acetic acid, the methyl keto acid obtained afforded a semicarbazone with a melting point (165-210°) different from the above. This on repeated crystallisations afforded a small quantity of the semicarbazone melting at 183-85°. Further, both the semicarbazones (m.p. 183-85° and m.p. 218.5 - 220°) analysed for $C_{16}H_{27}O_3N_3$ but their infrared spectra were not superimposable. However, the methyl esters of the ketoacids obtained after regeneration from the respective semicarbazones and esterification showed very similar infrared spectra but their PMR spectra (Fig.3 and 4) exhibited striking differences. Thus, the ester corresponding to the lower melting semicarbazones recorded a signal at 123 cps assignable to the $CH_3.CO$ group, while the ester corresponding

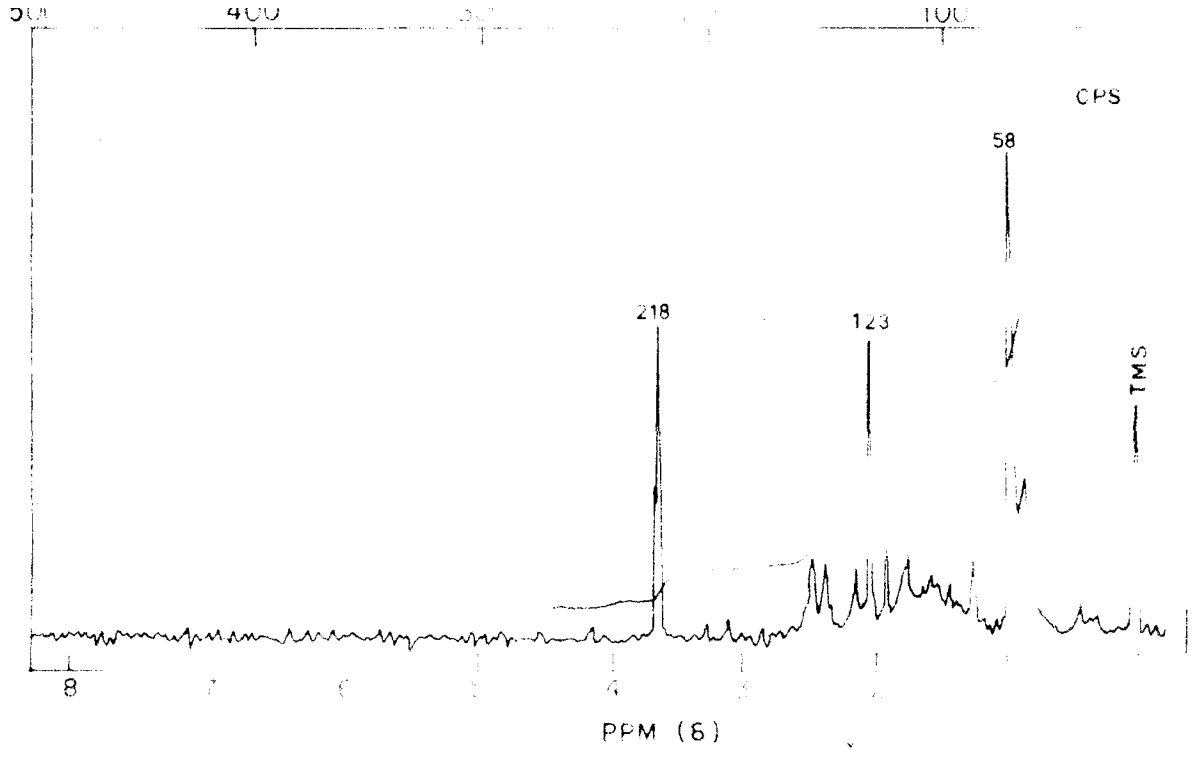


FIG. 3. PMR SPECTRUM OF THE METHYL ESTER OF THE KETO ACID XVIIa (Unstable epimer)

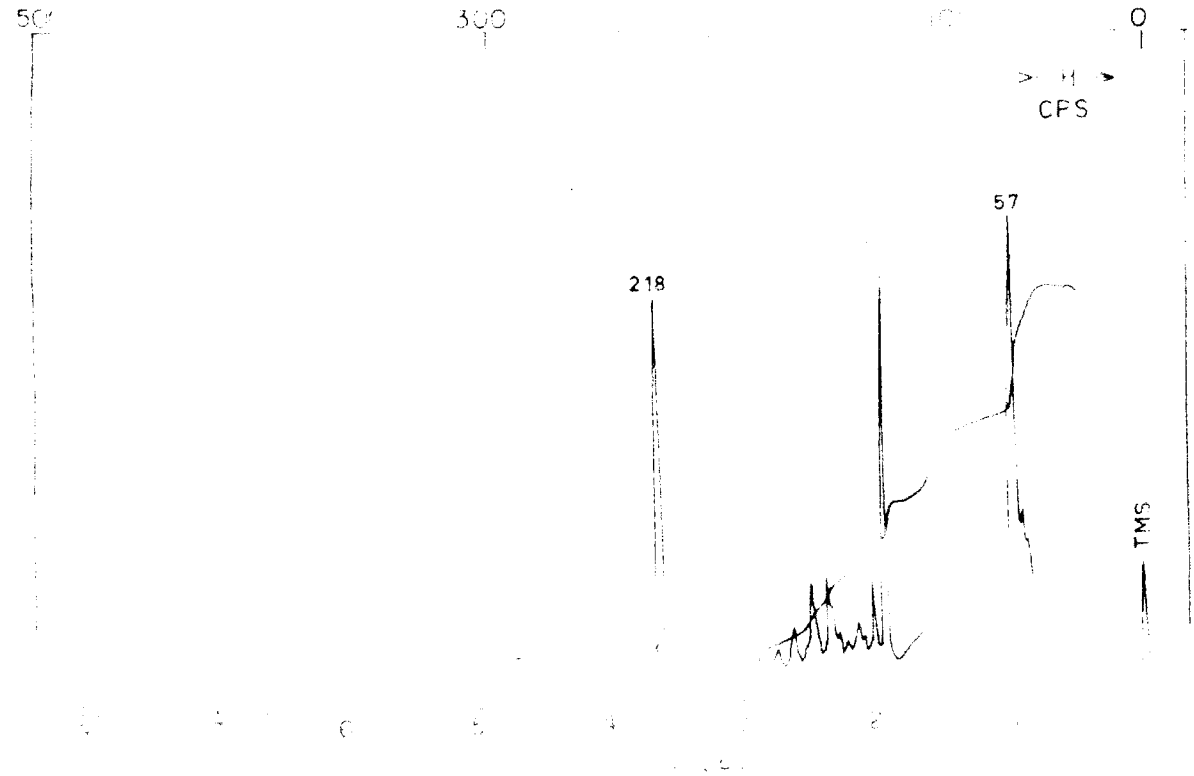
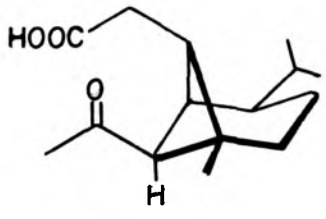


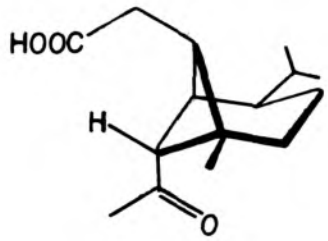
FIG 4. PMR SPECTRUM OF THE METHYL ESTER OF THE (Stable epimer)

to the higher-melting semicarbazone recorded a signal assignable to the same acetyl group at 115 cps. Further the keto-acid obtained from the regeneration of the lower-melting semicarbazone was completely isomerised by treating it with a base to the keto acid affording the high-melting semicarbazone.

Since the initial oxidation product from (XIV) must have the configuration XVIIa this must be unstable relative to its epimer XVIIb the product of base equilibration. This preference of the bulkier acetyl group (at C_2) to move into the axial confirmation must be attributed to the 1,3-diaxial-type interactions between the $-CO.CH_3$ and the $-CH_2.COOH$ groups on C_2 and C_6 respectively, in XVIIa, and this is expected to outweigh the resulting 1,3-diaxial interactions in XVIIb.



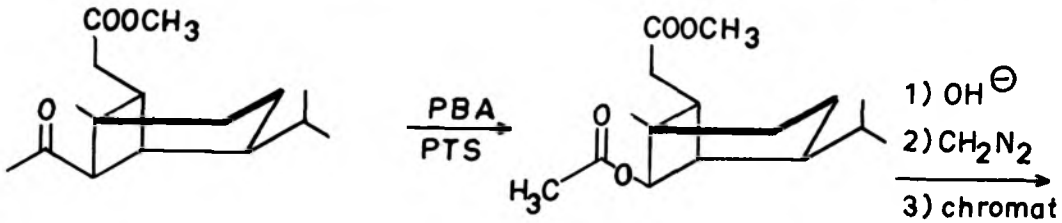
XVIIa



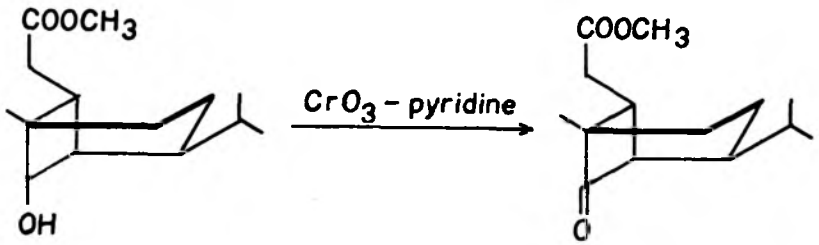
XVIIb

The methyl ester (XVII) of the (stable) keto-acid when subjected to perbenzoic acid oxidation in chloroform in the presence of some p-toluene sulphonic acid yielded the corresponding diester (XVIII). The diester on alkaline

hydrolysis and re-esterification followed by chromatography yielded the hydroxy ester XIX. This hydroxy ester (XIX) on CrO_3-pyridine oxidation yielded the keto ester, which as required on the basis of XIV should be a cyclobutanone (XX), a fact borne out by its IR spectrum: ν^{CHCl_3} 1780 cm^{-1} (Fig.5).



XVII XVIII



XIX XX

This degradation, along with its known conversion to cadinene dihydrochloride on reaction with hydrochloric acid gas, suffices to establish the structure IV for COPAENE.

Stereochemistry

Because of the bridged structure for copaene, the only points of stereochemical interest which remain to be determined are the configuration at C_{10} and the absolute stereochemistry. Both of these are settled

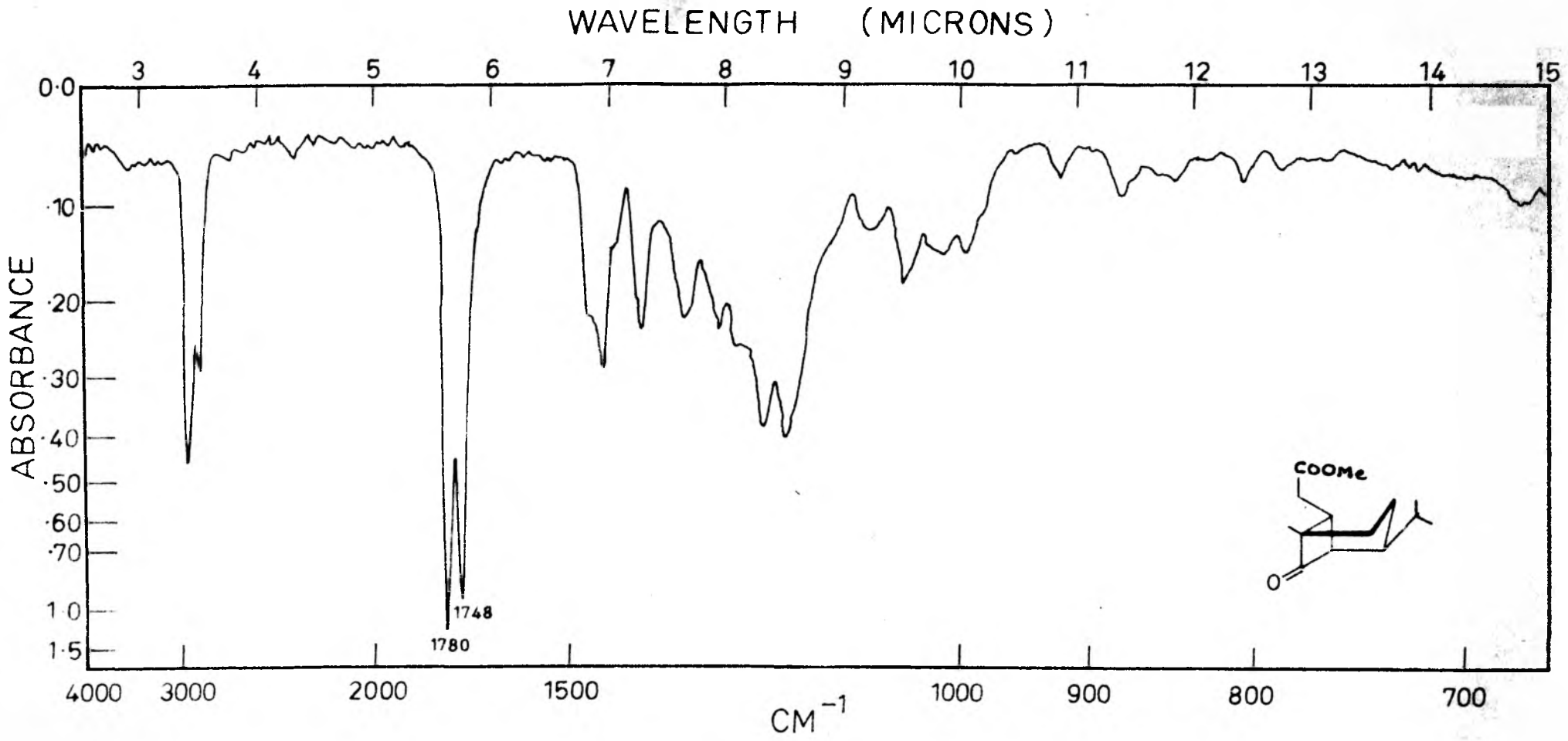


FIG. 5. IR SPECTRUM OF THE CYCLOBUTANONE DERIVATIVE (XX)

uniquely by the fact that (-)-copaene on treatment with hydrochloric acid gas, furnishes (-)-cadinene dihydrochloride (XIV) of established absolute stereochemistry[17]. Since configurations at C_1 and C_{10} are not involved in the cleavage reaction*, structure (XIV)

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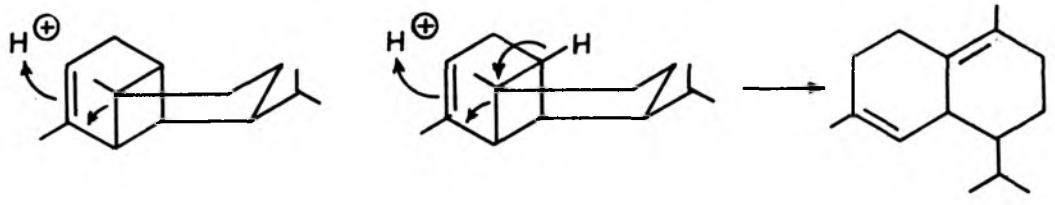
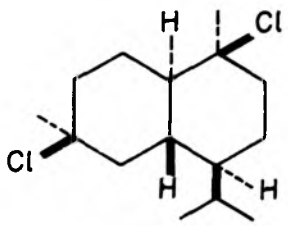
*Because of the key importance of this reaction, it has been rechecked with pure (-)-copaene, when 25% yield of crystalline (-)-cadinene dihydrochloride was obtained. The mother liquors on work up yielded a product ($[\alpha]_D$ -16.0) which analysed essentially for a dihydrochloride, and from its IR spectrum, consisted chiefly of a dihydrochloride different from cadinene dihydrochloride.

The ring-cleavage reaction if operating as shown (XXI), should give mostly a dihydrochloride with the two rings cis-locked (muurolene dihydrochloride[18]) while the formation of cadinene dihydrochloride would require either epimerisation at C_6 during the course of reaction (which is quite feasible) or else the direct opening as in XXII of copaene to XXIII. Since muurolenes give only muurolene dihydrochloride, a concerted one-step formation of XXIII (the hydrogen at C_6 and the C_2-C_7 bond have the required antiparallel geometry), may as well be the preferred route to cadinene dihydrochloride. This may also explain the absence of formation of any secondary monohydrochloride (in the PMR spectrum the hydrochloride from the mother liquor failed to show any absorption in the range expected for $>C<^{H}_{Cl}$) in the reaction which is in direct contrast to the behaviour of α-pinene and the closely analogous α-longipinene[19].



XXI XXII XXIII

should furnish (+)-cadinene dihydrochloride after ring-opening and hence the absolute configuration of (-)-copaene would be represented by the mirror image of XIV.



XXIV

E X P E R I M E N T A L

All m.p. and b.p. are uncorrected. Pet. ether refers to the fraction b.p. 40-60°. All solvent extracts were finally washed with brine, before drying (Na_2SO_4). Optical rotations were taken in $CHCl_3$. IR spectra were taken on a Perkin-Elmer Infracord, model 137 E, either as smears (liquids) or in nujol (solids). UV spectra were taken on a Perkin-Elmer Spectrophotometer, model 350, in 95% ethanol. All PMR spectra were taken in 10-20% solution in CCl_4 with tetramethylsilane as the internal standard, on a Varian Associates A-60 spectrometer; peaks are reported in cps from tetramethylsilane.

Alumina used for chromatography was made neutral by the HNO_3 method[20] and standardised according to Brockmann[21]. Thin-layer chromatography (TLC) was carried out on silica-gel containing 15% gypsum using equipment and procedure described elsewhere[22]; visualisation of the spots, after development was done by spraying with 33% chlorosulphonic acid in acetic acid and warming. Gas-liquid chromatography (GLC) was done on Perkin-Elmer Vapour Fractometer, model 154D, using H_2 as the carrier gas and a 2-meter column (internal diameter 1/4") packed with 20% diethylene glycol succinate on Chromosorb W.

Copaene

This was isolated from the essential oil from the

wood of Cedrela toona[23] by precise fractionation. The pure (GLC) material had: b.p. 112-113°/7.5 mm, n_D^{26} 1.4885, d_4^{26} 0.9055, M_D 64.98 (Calc. $C_{15}H_{24}$ 1 F 64.43), $[\alpha]_D^{30}$ -6.53 (c, 2.3%). IR spectrum: C=C 3010, 1660, 788 cm^{-1}.

Action of hydrochloric acid on copaene

Copaene (0.2 g) in dry ether (4 ml) was saturated with HCl gas at -10° and left as such at 0° overnight (15 hr). The solvent was removed (suction) and the residue taken up in pet. ether and the crystals collected after cooling at -15° for 1/2 hr; the product after recrystallisation from ethyl acetate had m.p. 114-115°, $[\alpha]_D$ -40.6°, mixed m.p. with an authentic sample (m.p. 116-117°) was undepressed, yield ~ 25%.

The solvent was removed from the original mother liquors and the residue distilled: b.p. (bath temp.) 180-200°/3 mm, $[\alpha]_D$ -15.6° (c, 1.2%). (Found: Cl 21.35%. $C_{15}H_{26}Cl_2$ requires: Cl 25.68%).

Dihydrocopaene (copane)

Copaene (0.5 g) was hydrogenated over pre-reduced PtO_2 catalyst (50 mg) in gl. AcOH (10 ml) at 25°/715 mm; hydrogenation was complete after the uptake of 0.98 mole of H_2 (1/2 hr). Usual work up and distillation gave the product as an oil, b.p. 105-106°/5 mm, n_D^{30} 1.4830 $[\alpha]_D^{30}$ = -2.31° (c, 2.2%). PMR spectrum: -CH($\underline{Me}_2$) 48, 53 cps; -CH$\underline{Me}$ doublet centred at 60 cps, J = 6 cps; quaternary methyl 60 cps.

Ozonolysis of copaene to ketocarboxylic acid

(i) Cleavage of the ozonide with alkaline hydrogen-peroxide

Copaene (5 g) in ethyl acetate (40 ml) was ozonised at ~-10° till ozone passed freely (3 hr; over ozonisation must be avoided). The solvent was removed under suction at room temp. and the residual syrup treated with water (25 ml), Na_2CO_3 (2.5 g) and hydrogen peroxide (30%, 5 + 5 ml) first at room temp. (1 hr) and later on a steam bath (2 hr). The product was separated into acidic (2.5 g) and neutral (2.5 g) portions. The acidic part was converted into its semicarbazone (pyridine method), m.p. 208-220° dec., yield 2.0 g; recrystallisation from ethanol gave a product, m.p. 218-220° dec. (Lit.[12], m.p. 221°), yield, 0.9 g.

The keto acid was regenerated from the above semicarbazone (1.9 g, m.p. 217-219°) by refluxing with oxalic acid (7 g), water (18 ml) and heptane (20 ml), with stirring for 3 hr. The product was worked up by extraction with benzene (30 ml x 4), washing and drying; solvent removal gave the required keto acid (1.61 g). The crude acid was converted into its methyl ester (CH_2N_2), which was distilled: b.p. 130-132°/0.5 mm, n_D^{30} 1.4750, $[\alpha]_D^{29.5}$ +61.5° (c, 6.0%). IR spectrum: >=O 1743, 1704 cm^{-1}. PMR spectrum: $COOCH_3$ 218 cps; $CO\underline{CH}_2$ 115 cps; quaternary methyl 57 cps; isopropyl methyl signals centred at 54 cps. (Found: C, 72.60; H, 10.03. $C_{16}H_{26}O_3$ requires: C, 72.18; H, 9.77%).

(ii) Cleavage of the ozonide with hydrogen peroxide in acetic acid: When the decomposition of the above ozonide (from 1g copaene) was carried out with hydrogen peroxide (10%, 10 ml) in acetic acid (5 ml), first at room temp. (1 hr), later at 60° (1 hr) and finally on steam bath (2.5 hr), and then worked up as above, 0.67 g crude acid was obtained, which was converted into the semicarbazone (0.52 g), m.p. 165-206°. Repeated recrystallisation (ethanol) of this material, finally gave 100 mg of a material m.p. 183-185° (Found: C, 62.23; H, 8.45. $C_{16}H_{27}O_3N_3$ requires: C, 62.13; H, 8.73%).

The keto acid was regenerated from this semicarbazone by the above procedure and the product esterified (CH_2N_2) and distilled: $[\alpha]_D^{33}$ +36.1° (c, 0.35%). IR spectrum: ν_{max} 1743, 1700 cm^{-1}. PMR spectrum: $COO\underline{CH_3}$ 213 cps; $CO\underline{CH_3}$ 123 cps; quaternary methyl 58 cps; isopropyl methyls centred at 54 cps.

The above keto acid (67 mg), after being refluxed with Na_2CO_3 aq. (10%, 1 ml) for 4 hr, was converted into its methyl ester, which was identified by its PMR spectrum as the product from (i). The isomerised keto acid gave the semicarbazone of m.p. 217-219°.

Baeyer-Villiger Oxidation of the methyl ester

The above keto ester (methyl ester of the keto acid regenerated from the semicarbazone m.p. 217-219°; 0.503 g) in $CHCl_3$ (8 ml) was treated with perbenzoic acid in $CHCl_3$

(7.35 ml containing 0.39 g ≡ 1.5 mole of per acid) and after adding p-toluene sulphonic acid (0.1 g), was left aside in the dark at room temp. (~30°). After 24 hr (in some experiments the reaction mixture had been allowed to stand for 7 days, without any adverse effect) it was found that one mole equivalent of the peracid had been used. The reaction mixture was worked up by washing it with Na_2CO_3 aq. (5%, 10 ml x 8), water (10 ml x 3), and drying. The solvent was flashed off to yield 0.559 g of a product, which was hydrolysed by refluxing with methanolic KOH (10%, 10 ml) for 2 hr. The solvent was completely removed and the residual K salt taken up in water (20 ml), acidified with H_3PO_4 and extracted with ether (30 ml x 3). The extracts were washed with water, dried and the solvent removed. The resulting crude hydroxy acid (0.477 g) was esterified (CH_2N_2) and the product distilled: b.p. 120-125°/ 0.5 mm, yield 0.34 g.

TLC (solvent system: 10% acetone in hexane) of the above product showed essentially two spots (starting material and product). The material (0.34 g) was chromatographed over Al_2O_3/ II (15 cm x 1 cm), while monitoring the eluterates with TLC:

Frac.1 :	Pet. ether	8 x 20 ml	35 mg of starting material.
Frac.2 :	Pet.ether/25% benzene.	7 x 20 ml	64 mg of mostly starting material.

Frac.3 :	Pet. ether/50% benzene.	5 x 20 ml	20 mg ?
Frac.4 :	Benzene	11 x 20 ml	105 mg of required compound.
Frac.5 :	Benzene/1% methanol	5 x 20 ml	50 mg of required compound.

Fractions 4 and 5, which were identical, as revealed by TLC and IR spectrum (OH 3410, 1100 cm^{-1}; -COOMe 1735 cm^{-1}) were mixed and had $[\alpha]_D^{30}$ +55.36° (c, 0.6%). The product was used as such for the next step.

Bis-nor keto ester (x)

The CrO_3-pyridine complex[24] (CrO_3 0.187 g, pyridine 2 ml) at ~25°C the above hydroxy ester (0.150 g) in 2.5 ml pyridine was added and the reaction mixture set aside as such for 16 hr. The product was diluted with water (10 ml) and extracted with benzene-ether (1:1; 10 ml x 4). The combined extracts were washed with water, $NaHCO_3$ aq. (5%) and water (10 ml x 2). After drying, the solvent was removed and the product distilled: b.p. (bath temp.) 150-160°/0.5 mm, n_D^{30} 1.4718, $[\alpha]_D^{31}$ + 38.4° (c, 0.38%). PMR spectrum: quaternary methyl 53 cps; isopropyl, a pair of doublets centred at 54 and 56 cps, each with J = 6 cps; -COOMe 220 cps. (Found: C, 70.33; H, 9.34. $C_{14}H_{20}O_3$ requires: C, 70.50; H, 9.24%).

SUMMARY

In connection with the structure determination of cyperotundone, a sesquiterpene ketone from Cyperus rotundus Linn. it became apparent that the currently accepted structure of copaene, a tricyclic sesquiterpene hydrocarbon, first isolated in 1914, was untenable. Evidence is now presented which permits the derivation of the absolute stereostructure of copaene.

REFERENCES

1 L.H.Briggs and R.C.Taylor, J. Chem. Soc. 1338 (1947).

2 (a) F. Vonasek, V. Herout and F.Sorm, Coll. Czech. Chem. Comm. 25, 913 (1960).

(b) V. Herout and V.Sykora, Tetrahedron 4, 246 (1958).

3 D.H.R.Barton and C.R.Narayanan, J. Chem. Soc. 963 (1958).

4 J.L.Erskine and E.J.Waight, J. Chem. Soc. 3425 (1960).

5 R.N.Jones, A.R.H.Cole, J. Am. Chem. Soc. 74, 5648 (1952).

6 R.N.Jones, A.R.H.Cole and B. Solin, Ibid. 74, 5662 (1952).

7 P. de Mayo and H. Takeshita, Canad. J. Chem. 41, 440 (1963).

8 (a) R.B. Woodward, J. Am. Chem. Soc. 63, 1123 (1941)
64, 76 (1942).

(b) L. Mortman, Chem. Rev. 53, 60 (1953).

9 Schimmel and Co. Ber. Schimmel p.48 April (1914).

10 F.J.Semmler and H. Stenzel, Ber. Dtsch. Chem. Ges. 47, 2555 (1914).

11 J.G.Henderson, A.M'Nab and J.M.Robertson, J.Chem. Soc. 3077 (1926).

12 A.J. Birch, Rep. Progr. Chem. 47, 135 (1951).

13 P. de Mayo, Perfum. essent. oil Rec. 49, 238 (1958).

14 R.N.Moore and G.S.Fischer, J. Am. Chem. Soc. 78, 4632(1956).

15 P. de Mayo, J.R.Robinson, E.Y.Spencer and R.W.White, Experientia 18, 359 (1962).

16 L.J. Bellamy, The Infrared spectra of complex molecules pp. 387-389, Methuen London 1958.

17 V.Sykora, V. Herout and F.Sorm, Coll. Czech. Chem. Comm. 23, 2131 (1958).

18 L.Westfelt, Acta Chem. Scand. 18, 572 (1964).

19 H. Erdtman and L. Westfelt, Acta Chem. Scand. 17, 2351(1963).

20 E. Lederer and M. Lederer, Chromatography, p.24, Elsevier Publishing Co., New York (1957).

21 H. Brockmann and H. Schodder, Ber. 74, 73 (1941).

22 A.S.Gupta and Sukh Dev, J. Chromatography 12, 189 (1963).

23 P.P.Pillai and B.S.Rao, J. Soc. Chem. Ind. Lond. 50, 220T (1937)

24 G.I. Poos, G.E.Arth, R.E.Beyler and L.H. Sarett, J. Am. Chem. Soc., 75, 425 (1953).

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B. A. Nagasampagi.

Poona 8

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