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TRANSFORMATION PRODUCTS OF TERPENOIDS

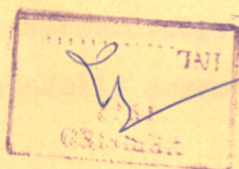
A THESIS SUBMITTED TO THE UNIVERSITY OF POONA
FOR THE DEGREE OF MASTER OF SCIENCE
IN CHEMISTRY

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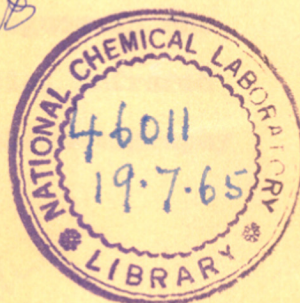
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POONA.

(JUNE, 1965.)

ACKNOWLEDGMENT



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A handwritten signature in cursive script, appearing to read "V. M. Sathe".

V. M. Sathe

June 1965

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INTRODUCTION AND SUMMARY

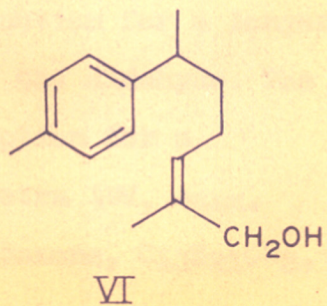
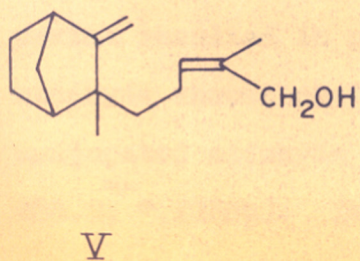
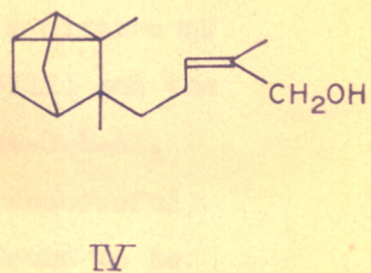
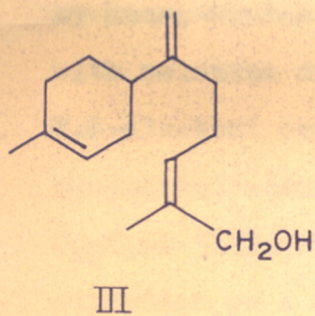
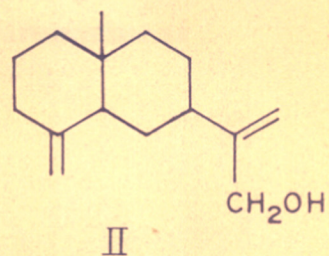
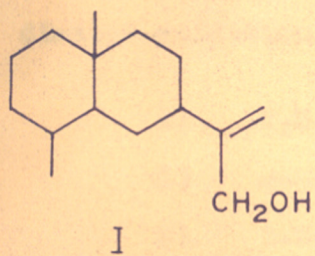
The present thesis deals with certain transformations in the sesquiterpene series. The objective of the investigation was to develop routes for the synthesis of some natural products via oxidation of suitable hydrocarbons with selenium dioxide as an oxidising agent at the initial stages. Selenium dioxide as an oxidising agent has certain interesting and attractive features. It was felt that though this reagent has been extensively used in organic chemistry, there was considerable scope left for extending its use for synthetic purposes in the terpene field.

Selenium dioxide is employed as a specific reagent for oxidising a methyl or a methylene group adjacent to a double bond, to an aldehydic or a ketonic function, the oxidation proceeding through the formation of an alcohol as an intermediate. This oxidation has been extensively used in terpene chemistry.¹ A survey of the present knowledge regarding the use of selenium dioxide as an oxidising agent is described in Part I of the thesis.

Many terpenoids contain in their molecules an isopropenyl or an isopropylidene group with a primary alcoholic function allylic to the double bond. Names of agarol² (I), costol³ (II), lanceol⁴ (III), α -santalol⁵ (IV), β -santalol⁵ (V), nuciferol⁶ (VI) may be cited as examples. In the case of alicyclic alcohols such as costol and agarol, the double bond exists in the isopropenyl form whereas in lanceol, santalols, nuciferol etc. in which the alcohol group is at the end of a long chain, it is the isopropylidene form which predominates or is the exclusive product. As several such interesting alcohols occur in nature, it was of obvious interest to develop methods of synthesis of such products by oxidation of the appropriate hydrocarbons with selenium dioxide, followed by reduction wherever required. With this objective in view, several suitable hydrocarbons have been oxidised resulting in the syntheses of several aldehydes and alcohols including some natural products.

In Part II of the thesis preparation of several hydrocarbons containing suitable double bonds and their subsequent oxidation with selenium dioxide has been described.

CHART 1.



SUMMARY OF PRESENT WORK

In the present work we have studied the selenium dioxide-oxidation of four different hydrocarbons:

- 1) 2,6-Dimethyl octene-2
- 2) α -Santalene
- 3) β -Santalene
- 4) Tetrahydro- β -elemene.

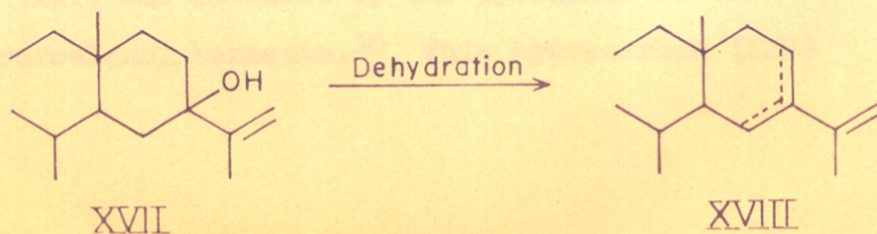
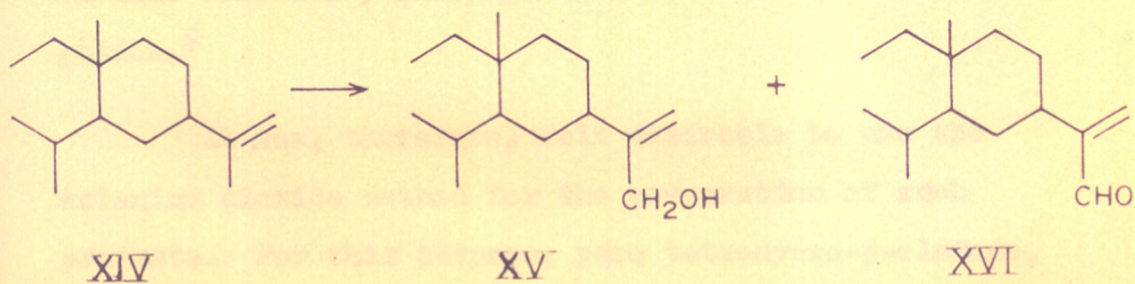
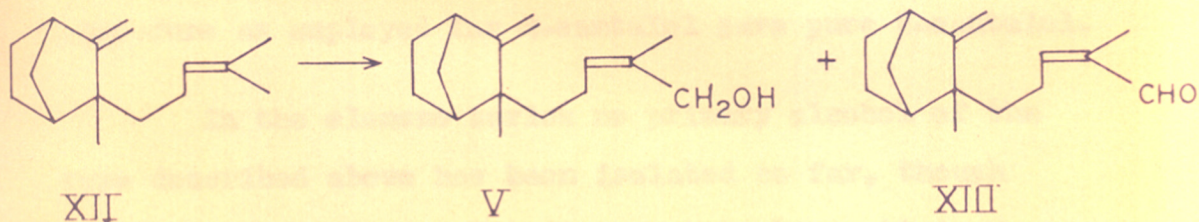
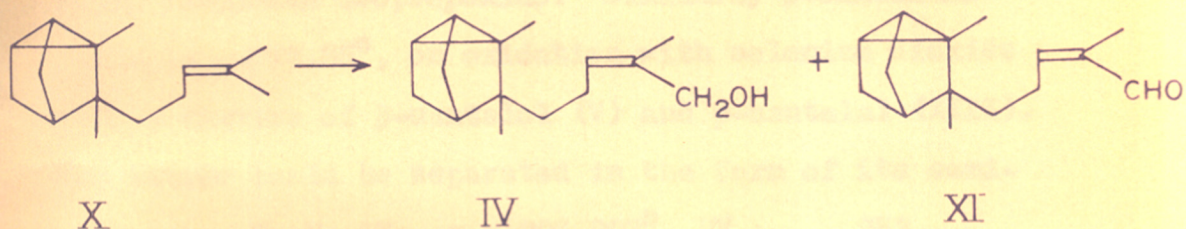
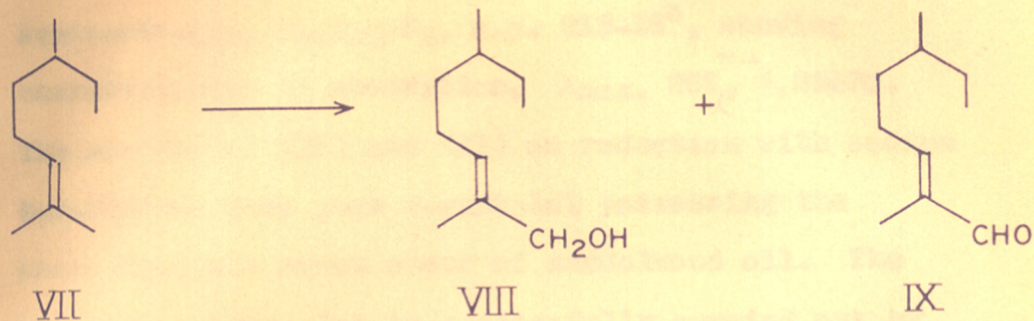
2,6-Dimethyl octene-2, $C_{10}H_{20}$ (VII) prepared⁷ by Huang-Minlon reduction of citronellal, on oxidation with selenium dioxide in ethanol gave a mixture of 2,6-dimethyl octene-2-1-ol, $C_{10}H_{20}O$ (VIII) and the conjugated aldehyde 2,6-dimethyl octene-2-1-al, $C_{10}H_{18}O$ (IX). The optimum period for successful oxidation on a boiling waterbath was found to be one hour. This was determined by carrying out a large number of experiments and examining the reaction products by VPC, IR and UV spectral studies. It was also observed that continuing the reaction for a longer period resulted in polymerisation of the aldehyde. The aldehyde showed characteristic absorption for a conjugated aldehyde in IR and UV spectra (UV, λ_{max} . 228.5; ϵ , 13900). It formed a semicarbazone, $C_{11}H_{21}ON_3$,

m.p. 177-78^o, showing UV absorption of a conjugated diene system, λ_{max} . 263 m μ , ϵ , 27520. With a view to obtain the alcohol (VIII) in a pure state, the mixture of (VIII) and (IX) was initially reduced with lithium aluminium hydride but the resulting product on careful examination by IR spectral studies and gas chromatography was found to be a mixture of unsaturated alcohol (VIII) and saturated alcohol, the latter being formed by simultaneous reduction of the double bond conjugated to the aldehyde function. Pure alcohol (VIII), however, could be successfully obtained by carrying out the reduction with sodium borohydride and also with aluminium hydride.

α - and β - Santalenes⁸ are the two main sesquiterpenic hydrocarbons occurring in East Indian sandalwood oil. Large quantities of these two hydrocarbons are obtained as by-products in sandalwood oil industry. As such these two hydrocarbons are not of much use to the perfumery industry. Conversion of these two hydrocarbons, therefore, to the industrially important alcohols α - and β - santalols is an attractive proposition. α -Santalol is the main odorous constituent of the East Indian sandalwood oil and forms about 60% of the total weight of the oil.

α -Santalene (X), (α)_D + 6.37^o, on oxidation with selenium dioxide gave a mixture of α -santalol(IV) and α -santalal (XI).

CHART 2.



The aldehyde, α -santalal (XI) was characterised as its semicarbazone, $C_{16}H_{25}ON_3$, m.p. $215-16^\circ$, showing characteristic UV absorption, $\lambda_{max.} 262, \epsilon, 35570$.
 The mixture of (IV) and (XI) on reduction with sodium borohydride gave pure α -santalol possessing the characteristic sweet odour of sandalwood oil. The reduction could also be successfully carried out by using aluminium isopropoxide. Similarly β -santalene (XII), $(\alpha)_D - 72.86^\circ$, on oxidation with selenium dioxide gave a mixture of β -santalol (V) and β -santalal (XIII). The latter could be separated in the form of its semicarbazone, $C_{16}H_{25}ON_3$, m.p. $206-207^\circ$, UV $\lambda_{max.} 263, \epsilon, 37010$. The reduction of the mixture by adopting the procedure as employed for α -santalol gave pure β -santalol.

In the elemene series no primary alcohol of the type described above has been isolated so far, though some related products of this type have been obtained in this laboratory in connection with another investigation.⁹

It was, therefore, felt desirable to use the selenium dioxide method for the preparation of such products. For this purpose, pure tetrahydro- β -elemene, $C_{15}H_{28}$ (XIV) was obtained by the pyrolysis of the tetrahydroelemol benzoate.¹⁰ This hydrocarbon (XIV)

on oxidation with selenium dioxide gave a mixture of the alcohol (XV) and the aldehyde (XVI). The aldehyde was characterised by the formation of a semicarbazone, $C_{16}H_{29}ON_3$, m.p. 208-209° with UV absorption, λ_{max} . 260.5 μ , ϵ , 21350. The mixture of (XV) and (XVI) on reduction with aluminium isopropoxide gave the pure alcohol (XV). Besides the alcohol (XV), a tertiary alcohol (XVII) also appears to be formed as a by-product. This undergoes dehydration resulting in the conjugated diene (XVIII), the formation of which is supported by IR and UV spectra.

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10. V. Sykora, V. Herout and F. Sorm, *Coll. Czech. Chem. Commun.*, 21, 267 (1956).

GENERAL REMARKS

1. All the melting points and boiling points are uncorrected and are recorded on centigrade scale.
2. Specific rotations were taken in chloroform solution unless otherwise stated.
3. Neutral alumina for chromatography was prepared from commercial aluminium hydrate (100-230 mesh) by washing with nitric acid, followed by water until free from acid, and then activated by heating at 400-450° for 6 hours.¹ Gradation of the active alumina was accomplished by mixing with requisite amount of water² and homogenising over a roller mill for 6 hours.
4. The infrared spectra were recorded as liquid film or in nujol suspension on a Perkin-Elmer Infracord Spectrophotometer, Model 137B, with sodium chloride optics.
5. The ultraviolet spectra were measured in ethanol solution on a Beckman ratio-recording spectrophotometer, Model DK-2.
6. Vapour phase chromatography analyses were carried out on Griffin VPC apparatus, MK-IIA with polyester column, using hydrogen as the carrier gas.
7. The numbers given to the charts and structures in each part of the thesis refer only to that particular part.

1. C. Djerassi, W. Rittel, J. Amer. Chem. Soc., 79, 3528 (1957).

2. E. Lederer, M. Lederer, 'Chromatography', Elsevier Pub. Co., New York, p. 26 (1957).

P A R T I

SELENIUM DIOXIDE AS AN OXIDISING AGENT

The first practical application of selenium dioxide for the oxidation of organic compounds was made in 1929, when Filip Kacer¹ found that 2-methyl benzanthrone could be oxidised to benzanthrone-2-carboxaldehyde by the action of selenium dioxide. Although selenium dioxide was in use since long, the specific nature of its oxidising action was not known. Schmidt² discovered that the oxidation of anthraquinone and its derivatives by the action of commercial fuming sulphuric acid was due to the catalytic action of selenium which was present as trace impurities in the acid. Soon afterwards, a number of workers like Riley, Morley, Friend, Melnikov, Rokitskaya and Guillemonat undertook a systematic study of the oxidising action of selenium dioxide and made extensive contributions towards the present knowledge of selenium dioxide oxidation.

Selenium dioxide has been extensively employed in a number of organic reactions. It has been widely used in reactions with compounds having different types of aromatic, aliphatic, alicyclic and heterocyclic systems. It has also been employed with remarkable success in organic compounds such as alkaloids, steroids, fatty oils, terpenes and other natural products. A number of organic

compounds which are not easily available in nature or which can be prepared with great difficulty have been synthesised by use of selenium dioxide.

Selenium dioxide is a mild and selective type of oxidising agent. It is used mainly for the oxidation of organic compounds having a reactive methyl or methylene group. Although it is reported that some compounds having no reactive methyl or methylene group are oxidised by this reagent, much importance cannot be attached to such reactions because they require high temperatures and the yields also are low. A reactive methyl or methylene group in an organic compound is oxidised by selenium dioxide, the methyl group being converted into a primary alcohol or an aldehyde (and sometimes an acid) and the methylene group into a secondary alcohol or a ketone. Excepting in a few cases, the seat of activation remains unaffected by the action of selenium dioxide and the cleavage of C-C link has so far not been observed.

The activation of methyl or methylene group depends mainly on the presence of suitable neighbouring groups. It is a well established fact that when a methyl or methylene group has in its α position, a carbonyl group, or a double or triple bond, or an aromatic or heterocyclic system, the methyl and methylene groups are activated.

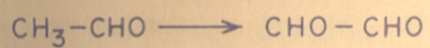
Effect of carbonyl group

Riley, Morley and Friend³ have shown that when an organic compound with a carbonyl function is treated with selenium dioxide, a methyl or methylene group in α position is oxidised and a 1,2-diketone or 1,2-dialdehyde or a 1,2-keto-aldehyde is produced.

Acetaldehyde³ (I) and acetone³ (III) which are carbonyl compounds of aliphatic series, undergo oxidation with selenium dioxide and give glyoxal (II) and methyl glyoxal (IV) in 90% and 60% yields respectively.

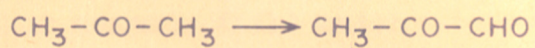
Cyclic ketones also undergo similar oxidation with selenium dioxide. Thus cyclohexanone³ (V) gives 1,2-cyclohexane dione (VI). Oxo-derivatives of hydroazulenes give 1,2-dioxo compounds. For instance, 4-oxo-1,2,3,4,5,6,7,8-octahydroazulene (VII)⁴ on treatment with selenium dioxide gives 4,5-dioxo-1,2,3,4,5,6,7,8-octahydroazulene (VIII). Among the terpenes, carvone and camphor are typical examples. Carvone⁵ (IX) has three active centres and undergoes oxidation with selenium dioxide in a complicated way. One of the oxidation products, however, shows that the methylene adjacent to the carbonyl is oxidised to give a 1,2-diketone (X) which subsequently enolises to give a hydroxy ketone (Xa). In the case of camphor⁶ (XI)

CHART I.



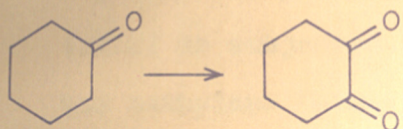
I

II



III

IV



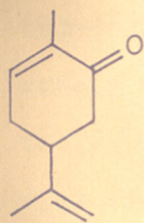
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VI

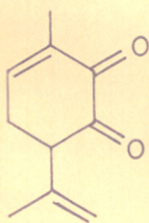


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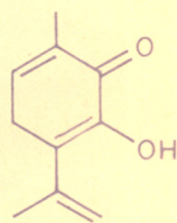
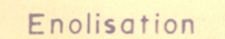
VIII



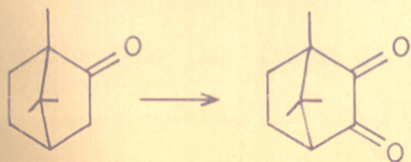
IX



X

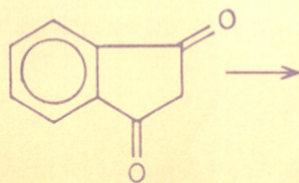


X_a



XI

XII



XIII

XIV

the oxidation product is camphor quinone (XII) which is a 1,2-diketone.

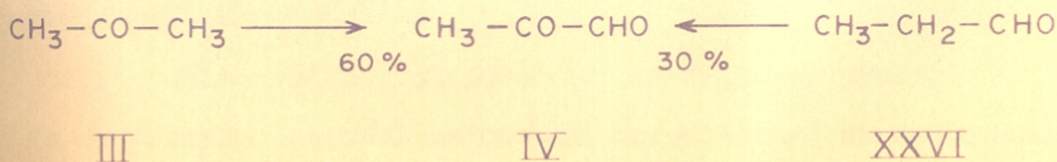
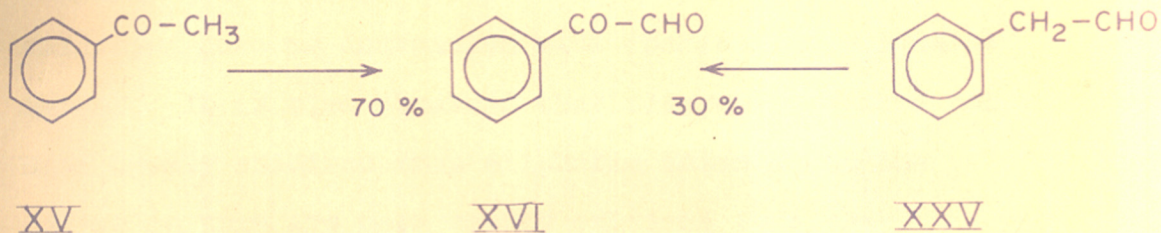
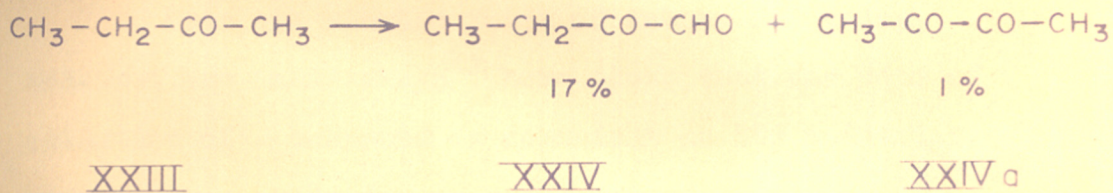
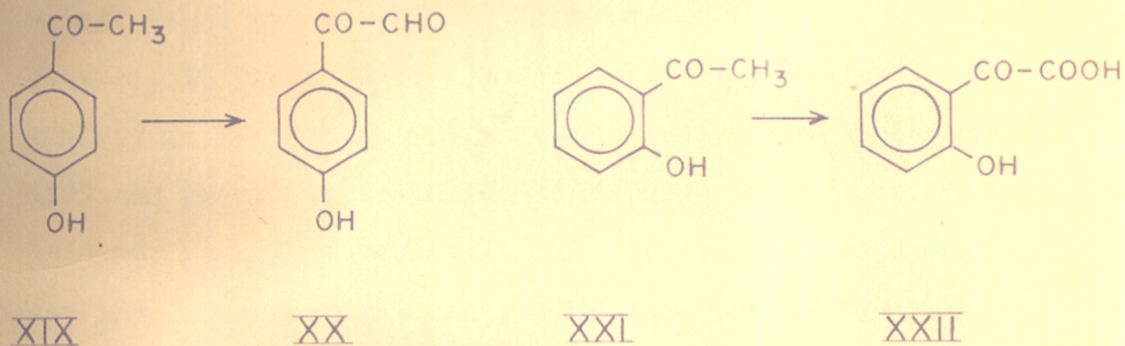
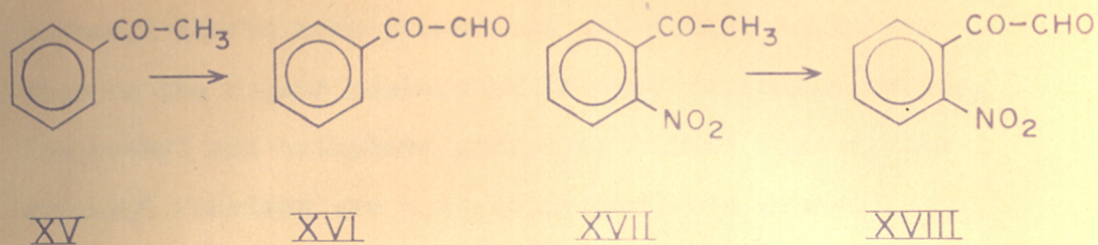
The synthesis of ninhydrin⁷ can be cited as a good illustration for the effect of carbonyl group on adjacent methylene groups. When 1,3-diketohydrindene (XIII) is subjected to the action of selenium dioxide, the methylene between the two carbonyl groups undergoes oxidation and ninhydrin (XIV) which is a diketo dihydroxy compound is produced.

Mixed type of alkyl-aryl ketones also exhibit the activating influence of the carbonyl function on adjacent methyl and methylene groups. Selenium dioxide reacts with acetophenone⁸ (XV) and gives phenyl glyoxal (XVI). Aryl substituted acetophenone derivatives also show similar behaviour. Thus *o*-nitro acetophenone⁹ (XVII) and *p*-hydroxy acetophenone¹⁰ (XIX) react with selenium dioxide to give *o*-nitrophenyl glyoxal (XVIII) and *p*-hydroxy phenyl glyoxal (XX).

If however *o*-hydroxy acetophenone¹⁰ (XXI) is used, the oxidation with selenium dioxide proceeds beyond the aldehyde stage and *o*-hydroxy glyoxallic acid (XXII) is produced.

Riley, Morley and Friend have shown³ from their work that in general, in lower aldehydes and ketones, the

CHART 2



carbonyl exerts more pronounced activating influence than in the higher members of the corresponding series. The methyl and methylene groups on either side of the carbonyl function are both activated, but methyl appears to be more active than methylene. Thus when methyl-ethyl ketone (XXIII) is oxidised by selenium dioxide, it gives ethyl glyoxal (XXIV) and biacetal (XXIVa) in 17% and 1% yield respectively. Acetophenone (XV) and phenyl acetaldehyde (XXV) give the same oxidation product, phenyl glyoxal (XVI) in 70% and 30% respectively and also acetone (III) and propionaldehyde (XXVI) give methyl glyoxal (IV) in 60% and 30% yield respectively.

From the kinetic study of ketone oxidation, Melnikov and Rokitskaya¹¹ have shown that the rate of oxidation of a compound is dependent on its molecular weight. The oxidation is comparatively rapid in compounds with lower molecular weight, and the rate of oxidation goes on decreasing with increase of molecular weight. It is also observed that alicyclic ketones are more easily oxidised than aliphatic ketones and the latter in turn are more easily oxidised than the aromatic ones.

Effects of unsaturation

Unsaturation, olefinic or acetylinic, present in an organic compound activates the α methyl or methylene

group in the compound. When such organic compounds are treated with selenium dioxide, the methyl group is oxidised to a primary allylic alcohol or a conjugated aldehyde. Similarly the methylene group is oxidised and a secondary allylic alcohol or a conjugated ketone is produced. Olefins with less than five carbon atoms generally do not¹² follow the rule of oxidation at α position.

Guillemonat¹³ has studied a great number of hydrocarbons in relation to the oxidising action of selenium dioxide and enunciated the following principles:

(1) The oxidation always occurs α to the more substituted end of the double bond.

(2) The order of preference for oxidation is
 $\text{CH}_2 > \text{CH}_3 > \text{CH}$.

(3) When there is a terminal double bond in an open chain compound, the oxidation proceeds in two different ways.

There also appears an additional rule¹⁴ in connection with the oxidation of closed chain compounds. It states that when there is a double bond in a ring, the oxidation occurs, whenever possible, in the ring itself.

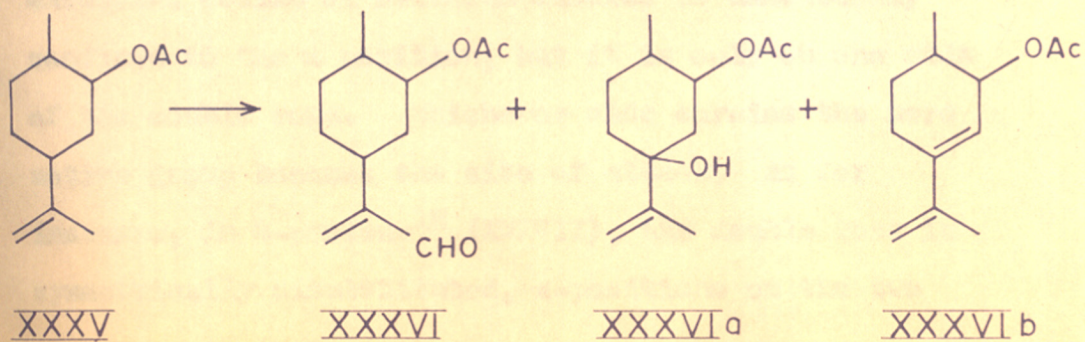
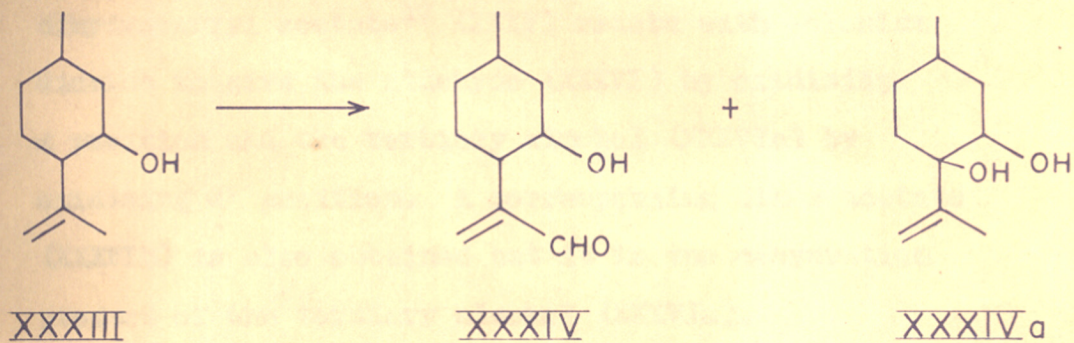
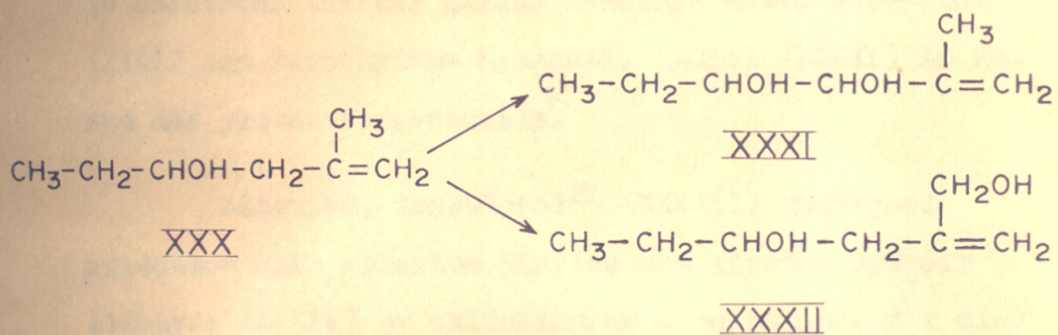
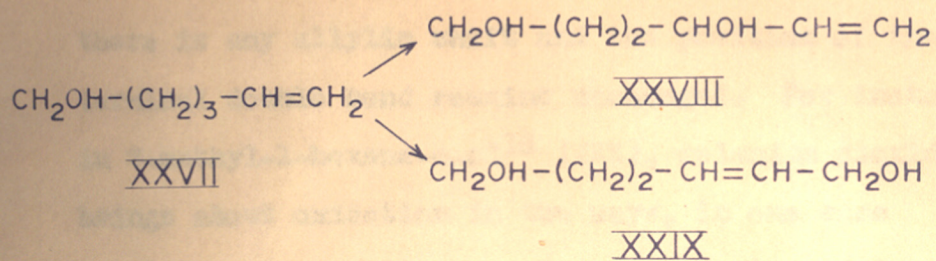
With the help of these guiding principles the oxidations in the following four possible types of cases of substituted alkenes can be considered.

- (1) Monosubstitution
- (2) Disubstitution
 - (a) Unsymmetrical
 - (b) Symmetrical
- (3) Trisubstitution
- (4) Tetrasubstitution

If the double bond is monosubstituted, the compound will be terminally unsaturated. Such a type of compound on treatment with selenium dioxide gives two isomeric alcohols, one in accordance with normal rules and the second, by allylic rearrangement. Thus 5-hexene-1-ol¹⁵ (XXVII) on treatment with selenium dioxide gives 5-hexene-1,4-diol (XXVIII) (17%) following normal rules and 2-hexene-1,6-diol (XXIX) (22%) by allylic rearrangement.

In the case of unsymmetrical disubstitution, the compound has a terminal double bond as in the case of monosubstituted double bond. If such a compound is treated with selenium dioxide two isomeric alcohols are obtained, in one case the oxidation is at α position and in another at α' position. But in neither case

CHART 3.

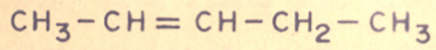


there is any allylic shift and the position of the terminal double bond remains unchanged. For instance, in 2-methyl-1-hexene-4-ol¹⁶ (XXX), selenium dioxide brings about oxidation in two ways, in one case α position is oxidised and in another α' position is oxidised, thereby giving 2-methyl hexene-3,4-diol (XXXI) and 2-methylene hexane-1, 4-diol (XXXII) in 54% and 46% yields respectively.

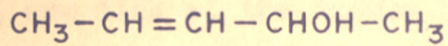
Likewise, isepulegol⁵¹ (XXXIII) undergoes oxidation with selenium dioxide and gives a hydroxy aldehyde (XXXIV) by oxidation at α position and a diol (XXXIVa) by oxidation at α' position. Similarly, dihydrocarvyl acetate¹⁷ (XXXV) reacts with selenium dioxide to give the aldehyde (XXXVI) by oxidising α position and the tertiary alcohol (XXXVIa) by oxidising α' position. A corresponding diene acetate (XXXVIb) is also obtained but it is the dehydration product of the tertiary alcohol (XXXVIa).

In the case of symmetrical disubstitution, the oxidising action of selenium dioxide is undoubtedly confined to the α position, but it is only on one side of the double bond. Whichever side carries the more active group becomes the site of attack. As for instance, in 2-pentene¹⁸ (XXXVII), the double bond is symmetrically disubstituted, α -positions on the two

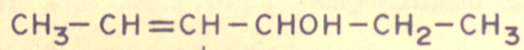
CHART 4.



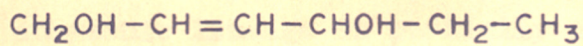
XXXVII



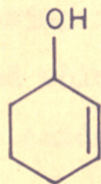
XXXVIII



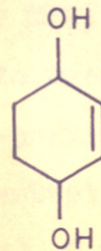
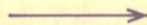
XXXIX



XL



XLI

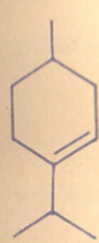
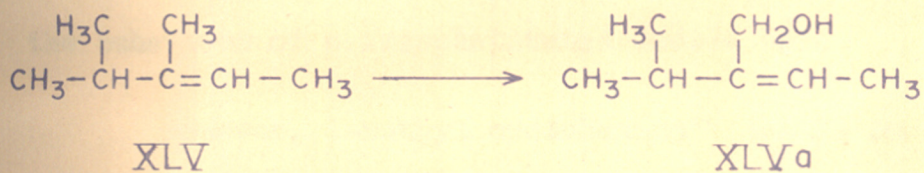
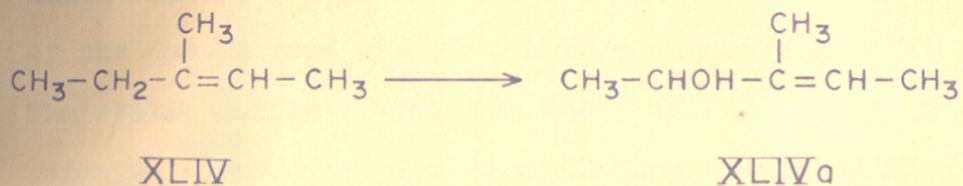
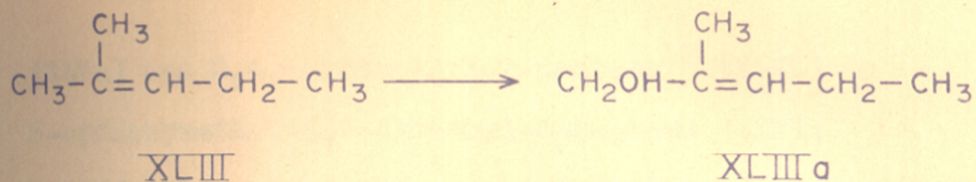


XLII

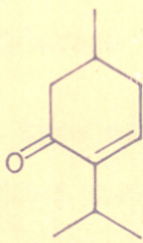
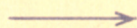
sides carrying methyl and methylene substituents. Oxidative attack by selenium dioxide will obviously be at the methylene site since the methylene group is more reactive than methyl group. The oxidation gives 2-pentene-4-ol (XXXVIII). In another case of 2-hexene-4-ol¹⁵ (XXXIX) where also there is symmetrical disubstitution, one side of the double bond carries a methyl substituent and another side, a methine substituent. As from the rules, methyl group is more reactive than methine group and consequently methyl group is oxidised and 2-hexene-1,4-diol (XL) is obtained. In the same way, 2-cyclohexenol¹⁶ (XLI) is oxidised by selenium dioxide to 2-cyclohexene-1,4-diol (XLII).

In the case of a trisubstituted double bond, one end of the ethylenic linkage is partially substituted and the other, fully substituted. When an organic compound with a trisubstituted double bond is treated with selenium dioxide, the α or α' position only on the fully substituted side of the double bond is oxidised. Here also the rule of decreasing activity in the order CH_2 , CH_3 , CH , is followed and whichever α or α' is more reactive gets oxidised. The oxidations of 2-methyl-2-pentene¹⁸ (XLIII) to 2-methyl-2-pentene-1-ol (XLIIIa), 3-methyl-2-pentene¹⁸ (XLIV) to 3-methyl-3-pentene-2-ol (XLIVa), 3,4-dimethyl-2-pentene¹⁸ (XLV) to 3-hydroxymethyl-4-methyl-2-pentene

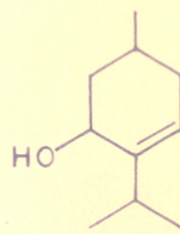
CHART 5.



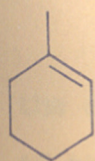
XLVII



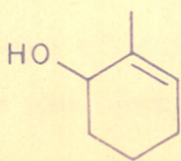
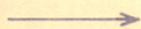
XLVIII



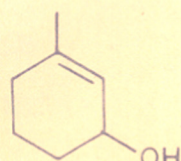
XLVIIIa



XLIX



L



La

(XLVa) and 3,4,4-trimethyl-2-pentene¹⁸ (XLVI) to 3-hydroxymethyl-4,4-dimethyl-2-pentene (XLVIa) justify the principles enunciated above that the oxidation takes place on the more substituted side of the double bond and at the more reactive substituent. The cyclic terpene p-menth-3-ene¹⁹ (XLVII) reacts with selenium dioxide to give p-menth-3-ene-5-one (XLVIII) and p-menth-3-ene-5-ol (XLVIIIa). This again explains the behaviour of a trisubstituted double bond.

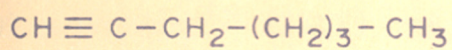
However, 1-methyl cyclohexene²⁰ (XLIX) on oxidation with selenium dioxide gives 1-methyl cyclohexene-3-ol (La) besides the normally expected oxidation product 1-methyl cyclohexene-6-ol (L).

If the double bond is tetrasubstituted the oxidation remains incomplete and the resultant mixture consists of several oxidation products.

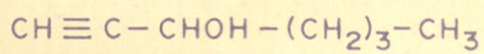
The acetylinic type of compounds undergo selenium dioxide oxidation generally in the same as way as the olefins. Thus 1-heptyne²¹ (LI) undergoes oxidation with selenium dioxide at α -methylene and gives 3-hydroxy-1-heptyne (LII).

A peculiar type of oxidation takes place in the case of olefinic and acetylinic type of compounds if there is no methyl or methylene group α to the double or triple bond. The olefinic or acetylinic

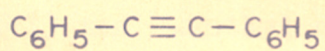
CHART 6.



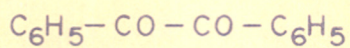
LI



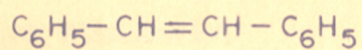
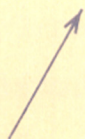
LII



LIII



LIV



LV

hydrogen, if there is any, is eliminated and a new oxygen function comes in with the conversion of double or triple bond into a single bond. Thus both diphenyl acetylene²² (LIII) and stilbene²² (LV) give benzil (LIV).

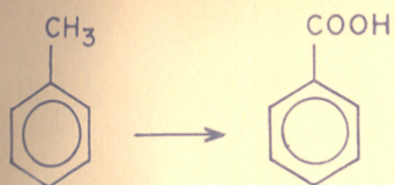
Effect of aromatic and heterocyclic systems

When an aromatic or an unsaturated heterocyclic system has a methyl or methylene group attached to the ring, an activating influence is exerted on the attached groups. On treatment with selenium dioxide, the methyl or methylene is oxidised to a carbonyl compound and in many cases acids are produced. Thus, toluene²³ (LVI) and 2-methyl naphthalene²⁴ (LVIII) on oxidation with selenium dioxide give benzoic acid (LVII) and 2-naphthaldehyde (LIX) respectively.

Similarly, diphenyl methane²⁵ (LX) gives benzophenone (LXI) and 2-phenyl ethyl alcohol²⁶ (LXII) gives phenyl glyoxal (LXIII). O-xylene²⁴ (LXIV) reacts with selenium dioxide to give a mixture of O-toluyaldehyde (LXV) and O-toluic acid (LXVI). The meta and para isomers behave similarly.

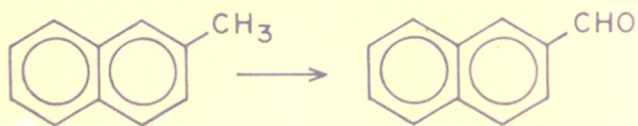
As in the case of aromatic system, unsaturated heterocyclic systems also exert activating influence on

CHART 7.



LVI

LVII



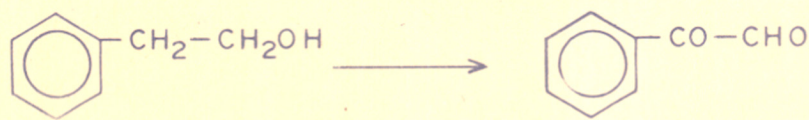
LVIII

LIX



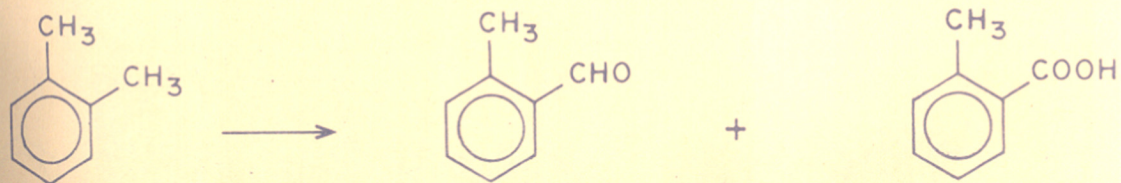
LX

LXI



LXII

LXIII

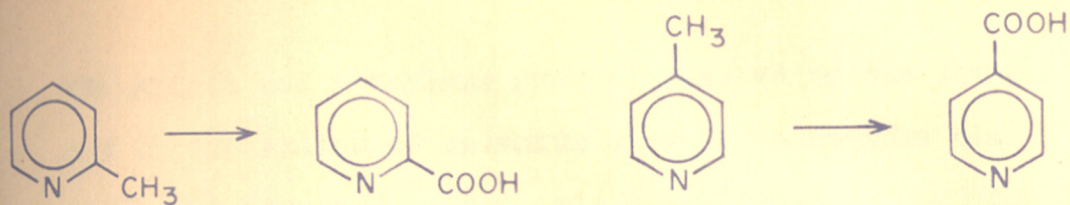


LXIV

LXV

LXVI

CHART 8.

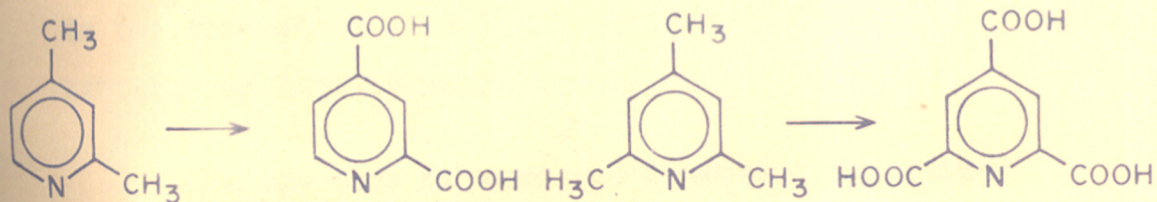


LXVII a

LXVIII a

LXVII b

LXVIII b

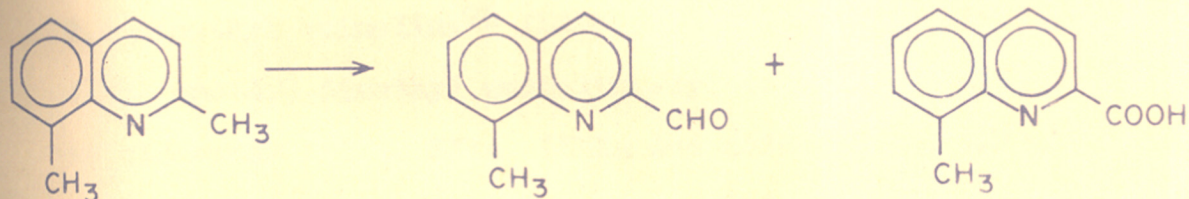


LXVII c

LXVIII c

LXVII d

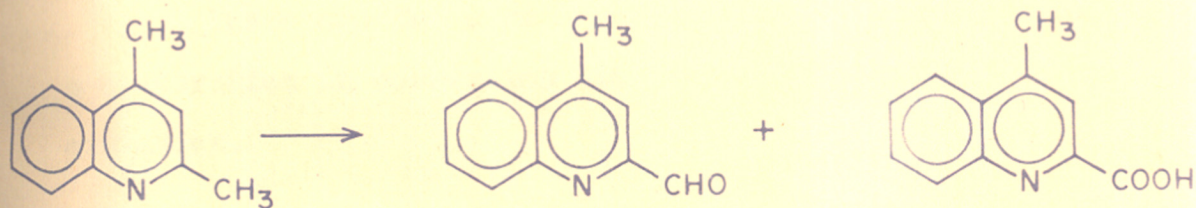
LXVIII d



LXIX

LXIX a

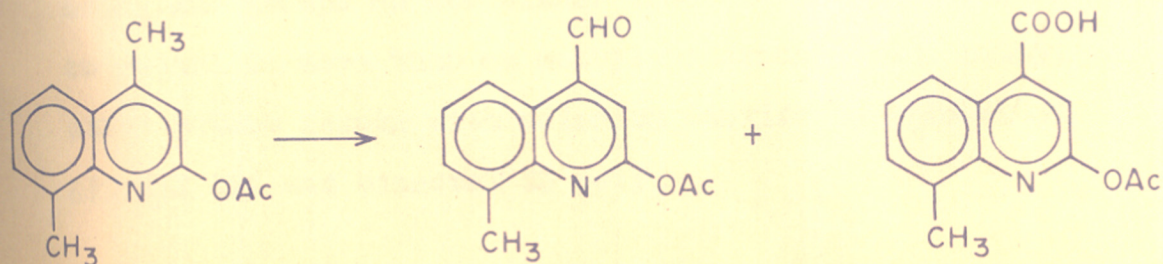
LXIX b



LXX

LXX a

LXX b



LXXI

LXXI a

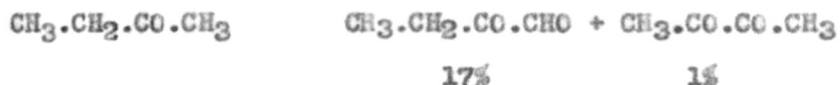
LXXI b.

the methyl and methylene groups attached to the system and by the action of selenium dioxide, aldehydes and acids are produced. Mono, di, and tri-methyl pyridines²⁷ as shown by LXVIIa, LXVIIb, LXVIIc, LXVIId react with selenium dioxide and all the methyl groups are oxidised to the acid stage with the formation of LXVIIIa, LXVIIIb, LXVIIIc and LXVIId respectively.

In the case of mono and di-methyl quinolines, the methyl at position 2 is preferentially oxidised and if there is no methyl at position 2, the methyl at position 4 is oxidised. The oxidations of compounds 2,8-dimethyl quinoline²⁸ (LXIX), 2,4-dimethyl quinoline²⁹ (LXX) and 4,8-dimethyl quinoline-2-yl-acetate³⁰ (LXXI) to aldehydes LXIXa, LXXa, LXXIa and acids LXIXb, LXXb, LXXIb respectively illustrate the point.

There are two more effects which deserve special consideration in connection with selenium dioxide oxidation.

It has been previously stated that a carbonyl function exerts activating influence both on methyl and methylene groups on its either side and that the effect on methyl is more than on methylene group. Thus methyl ethyl ketone reacts with selenium dioxide to give ethyl glyoxal 17% and biacetal 1% only.



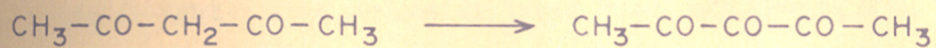
In the case of β -diketones and β -ketoesters, the methylene between the carbonyls is highly activated with the result that no reaction takes place at the methyl function. Thus selenium dioxide oxidises acetyl acetone³¹ (LXXII) and ethyl aceto-acetate³² (LXXIII) to the triketone (LXXIIa) and diketo ester (LXXIIIa) respectively.

In another type of oxidation by selenium dioxide, there is no introduction of oxygen but simple dehydrogenation takes place with simultaneous introduction of a double bond. When two methylene or methine groups or a methylene and a methine groups are present between two activating groups, the action of selenium dioxide brings about dehydrogenation at the methylene and methine groups and a double bond is introduced. This is well illustrated by oxidation of compounds LXXIV,³³ LXXV,³⁴ LXXVI,³⁵ and LXXVII³⁶ to LXXIVa, LXXVa, LXXVIa, and LXXVIIa respectively.

Effect of solvent and temperature variations

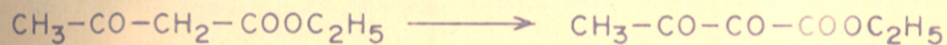
The most important factors which affect the selenium dioxide oxidation reactions are the nature of the solvent and the temperature employed for the reaction.

CHART 9.



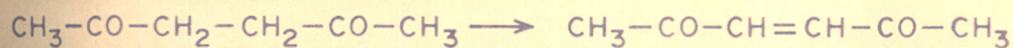
LXXII

LXXII a



LXXIII

LXXIII a



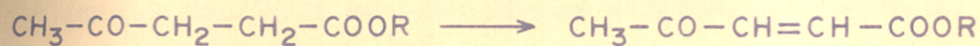
LXXIV

LXXIV a



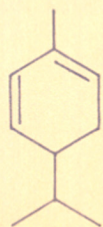
LXXV

LXXV a

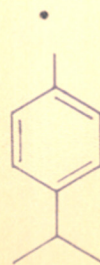
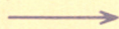


LXXVI

LXXVI a



LXXVII



LXXVII a

A review^{37,37a} of the literature shows that a great variety of solvents have been utilised. The list includes dioxane, acetic acid, acetic anhydride, ethanol, water, benzene, methanol, butanol, amyl alcohol, nitrobenzene, toluene, xylene, hexane, ether, carbon tetrachloride, pyridine, ethyl acetate, acetonitrile and various combinations of these solvents. Of these the first six have been used with much wider application and quite recently dimethyl sulphoxide has come into use. Acetic acid is claimed¹⁸ to exert favourable effect during selenium dioxide oxidation. But in many compounds it brings about isomerisation of double bonds. It also partially forms acetates by reacting with the hydroxy compounds obtained by oxidation so that the resultant product is a mixture of hydroxy compounds and acetates. Acetic anhydride is much superior in this respect as it does not form such mixtures of hydroxy compounds and acetates. Ethanol, in general, gives a smooth reaction but the yields are not substantial. In some cases, it is reported to form ethers by reaction with the oxidation products. The nature of the solvent employed also affects the yields of the oxidation product and this is illustrated^{38,39} in the following table.

Table

Compound	Solvent	Oxidation product	Yield %
Camphor	Ethanol	Camphorquinone	27
"	Toluene	"	89
"	Xylene	"	89
"	Acetic anhydride	"	95
"	No solvent	"	65

Similarly, 3-chlorocamphor^{38,40} is not attacked by selenium dioxide when acetic acid is the solvent but in the absence of any solvent, the oxidation product is camphorquinone.

Most of the selenium dioxide reactions are carried out at the boiling point of the solvent employed. An interesting effect of temperature variation is observed in the oxidation of 1,2,3,4,5,6,7,8 octahydronaphthalene.⁴¹ This is given in the table below.

Compound	Solvent	Temp.	Oxidation product
1,2,3,4,5,6, 7,8 Octahydro naphthalene	Acetic anhydride	0-5°	A
		25-30°	A + B
		70°	A+B+C
		120-124°	C

where A = 1,2,3,4,5,6,7,8 octahydro-1-naphthol acetate.
B = 1,2,3,4,5,6,7,8 octahydro-1,5-naphthalene diol-
diacetate.
C = 1,2,3,5,6,7 hexahydro-1,5-naphthalene diol-
diacetate.

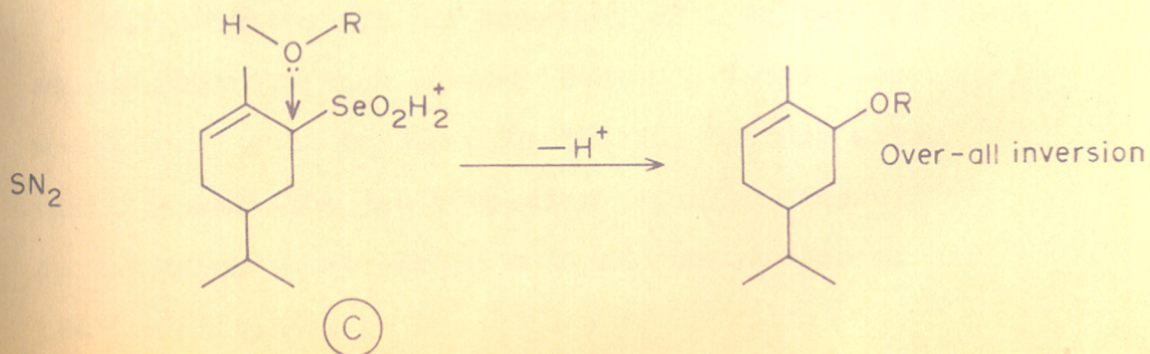
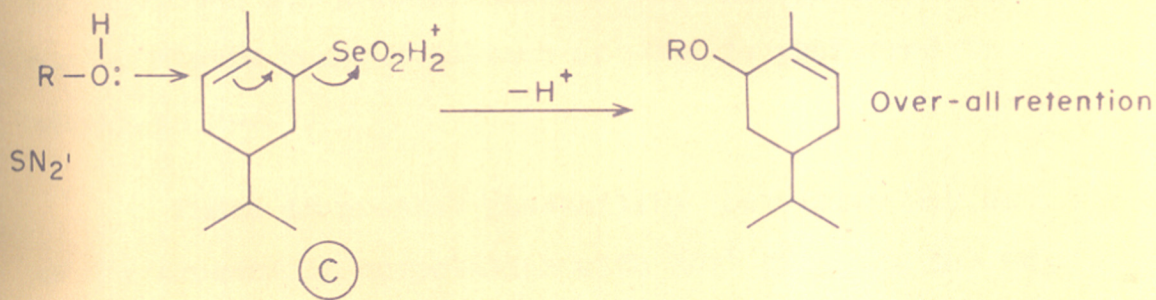
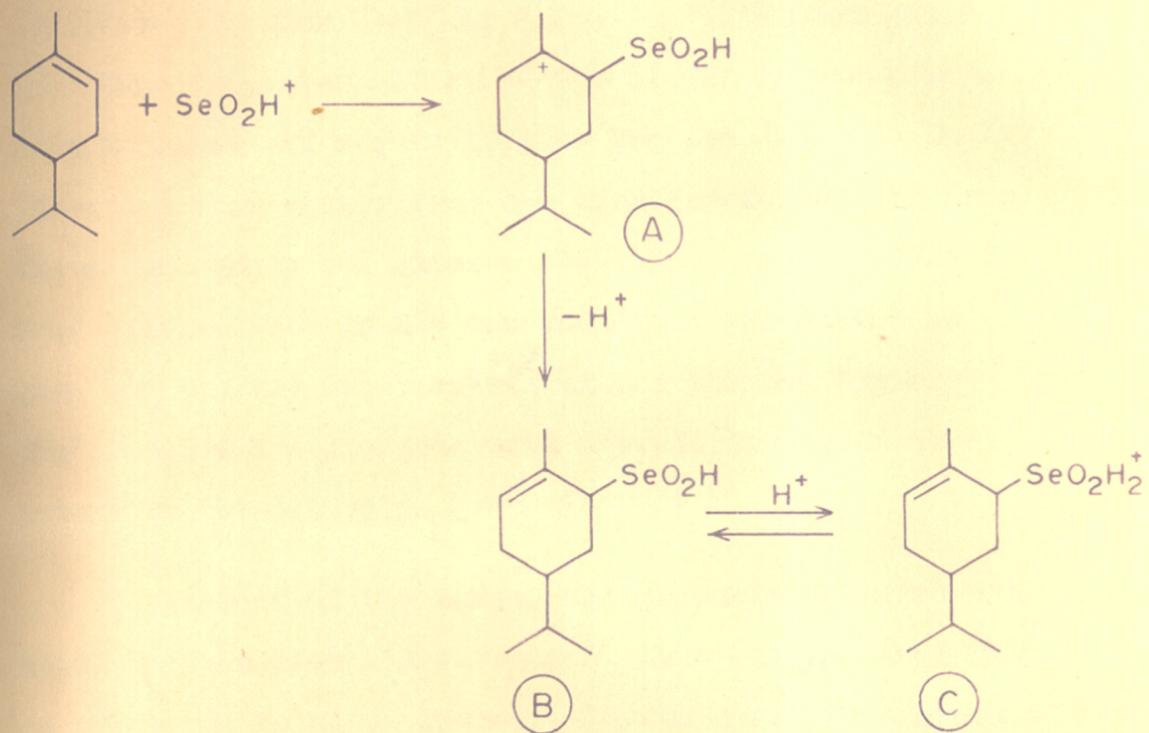
Mechanism of selenium dioxide oxidation

There are two different mechanisms suggested for two different types of compounds (1) unsaturated hydrocarbons, (2) carbonyl compounds.

As regards unsaturated hydrocarbons, Guillemonat¹⁸ postulated the theory of intermediate complex formation. He gave a rough outline of the course of reaction an unsaturated hydrocarbon would undergo during selenium dioxide oxidation. According to him, selenium dioxide was supposed to attack the reactive methyl or methylene group in an unsaturated hydrocarbon and form a complex without affecting the double bond. The complex was then supposed to undergo hydrolytic decomposition with the separation of selenium metalloid and formation of a conjugated aldehyde or a ketone.

The above picture was rather too crude to give a clear idea about the mechanism of oxidation reaction. Recently Wiberg and Nielsen⁴² made some observations on allylic oxidation and they have put forth a new mechanism for selenium dioxide oxidation of alkenes.

CHART 10.



According to them, selenium dioxide gets protonated to form HSeO_2^+ or H_3SeO_3^+ . This protonated body then initiates attack on the olefin in accordance with Markownikoff's rule to give the ion (A). The ion (A) loses a proton either from the ring (preferred) or from the methyl group and gives a stabilised intermediate (B). This intermediate in its own turn gets protonated to give the ion (C) which reacts either through SN_2 or SN_2' to give the products with overall inversion or retention respectively. (Vide, chart -10)

In most of the cases, the products obtained are found to have over all retention, thus showing that SN_2' is preferred to SN_2 . However, in the case of terminal olefins, the SN_2 process has the predominant influence due to steric reasons (attack on $-\text{CH}_2$ is preferred to attack on $\text{R}-\text{CH}$).

There is another possibility that there may be an SN_1 process in competition with SN_2' process. The SN_1 process would result in the formation of an allyl cation which would be planar and would be expected to yield a racemic product. In the presence of a solvent of lower nucleophilicity than aqueous ethanol, the SN_2 -process would largely be replaced by the SN_1 process which would explain the low retention actually observed⁴³ in the cases where acetic acid and moist dioxane are used as solvents.

For explaining the oxidation of carbonyl compounds, Melnikov and Rokitskya suggested⁴⁴⁻⁴⁹ the possible pathway involving enolisation, esterification and thermal decomposition of the ester ultimately leading to the formation of a dicarbonyl compound. These two workers have made numerous but rather rough kinetic measurements of the selenium dioxide oxidation of various aldehydes and ketones. They have reported that in all cases the reaction is of the second order. They noted parallelism between the rate of oxidation and rate of enolisation of carbonyl compounds. They also prepared dialkyl selenites from primary alcohols and selenium dioxide and observed that the thermal decomposition of the dialkyl selenites gave aldehydes. On the basis of this evidence it was postulated that the reaction path consisted of enolisation followed by the formation of the complex with selenium dioxide. The complex was supposed to subsequently decompose and give a dicarbonyl compound, selenium and water. It was also proposed that the relative degree of enolisation of a ketone could be ascertained from the rates of oxidation. These conclusions are, however, generally found to be incorrect.

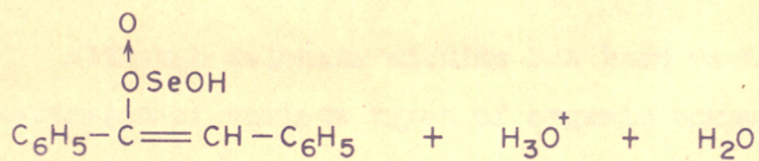
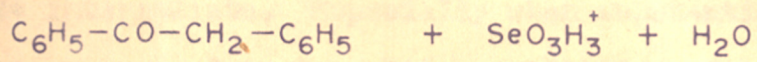
Corey and Schaefer⁵⁰ more rigorously investigated the mechanism by studying the course of selenium dioxide oxidation of desoxy benzoin and its derivatives

to benzils. By kinetic measurements, they found that oxidation of desoxy benzoin is of the second order. From the study they concluded that although the substituent effects are similar for enolisation and oxidation, enol is clearly not an important intermediate in the oxidation of desoxy benzoin as was formerly supposed to be the case. From the data they inferred that in the oxidation of a ketone by selenious acid the course of the reaction always proceeds by electrophilic attack on carbonyl oxygen with simultaneous or subsequent nucleophilic attack on the α hydrogen. Selenious acid is protonated and acts as an electrophile $H_3SeO_3^+$, and water, the available base acts as the nucleophile. By the electrophilic attack of $H_3SeO_3^+$ on carbonyl oxygen, an enol-selenite ester (A) is formed which isomerises to a selenium ester intermediate (B) by internal rearrangement which is subject to acid catalysis. The intermediate (B) which has bivalent selenium, loses selenious acid in the form of selenium and water by the process of 1,2-elimination and gives a diketone. (Vide chart-11)

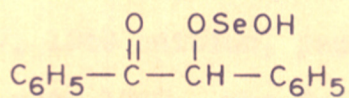
This course has been found to be followed in the case of almost all carbonyl compounds.

Although in the case of desoxy benzoin, the enol selenite ester is formed by direct electrophilic

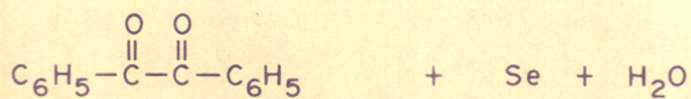
CHART 11.



(A)

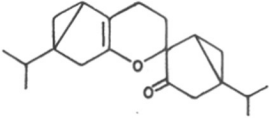


(B)



attack on carbonyl oxygen and not via the desoxy benzoin enol, there are some instances where enol is the intermediate. Especially when substantial amount of an enol is in mobile equilibrium with a ketone, the enol reacts with selenious acid to form an enol selenite which follows the same course as shown above and ultimately forms a diketone selenium and water.

Although selenium dioxide has been used for the oxidation of various types of organic compounds our interest has been mainly centred round terpenic compounds. A survey of the literature reveals that a variety of terpenes have been subjected to selenium dioxide oxidation and very interesting products have been obtained from them. A review of selenium dioxide oxidation by Norman Rabjohn in 'Organic Reactions' Vol.V, 1949 edition, page 331-386 covers up the work done upto 1947. The following table gives additional list of various terpenes subjected to selenium dioxide oxidation. The survey is only in respect of terpenes, extending over a period 1947 to 1965 January.

No.	Compound	Solvent	Product of oxidation	Reference
1.	Carvone	Ethanol	p-mentha-6,8(9) diene-1-al-2-one p-mentha-3,6,8(9) triene-3-ol	5
2.	Citronellal	Ethanol	2,6-dimethyl-2-en- 1,8-dialdehyde	5
3.	α -Pinene	Acetic anhydride	Myritinol (23%) Pinol (4.4%)	52
4.	α -Thujene	Ethanol	p-Cymene 4-isopropyl-1,3-cyclo- hexdiene-4-carboxal- dehyde	53
5.	Cadinene	Ethanol	Probably a dimer	54
6.	Limonene		Primary alcohol Secondary alcohol (both unidentified)	55
7.	p-Mentha-3- en	Ethanol	p-mentha-3-ene-5-one p-mentha-3-ene-5-ol	56
8.	Sabinol	Ethanol		57
9.	Camphene	Acetic anhydride	Camphene glycol carbonate	58
10.	Camphene	Δ -	Camphenilone Tricylol Carbocamphenilone	59

No.	Compound	Solvent	Product of oxidation	Ref.
11	β -terpineol- (p-mentha-8- en-1-ol)	Ac ₂ O + AcOH	8(9)-p-menthene-1-ol- 10-al Acetate of the above 3,8(9)-p-menthadiene- 1-yl-acetate	60
12.	β -terpineol (p-mentha-8-en- 1-ol)	tert. butanol + benzene	8(9)-p-menthen-1-ol- 10-al Acetate of above Trans-8(9) menthene- 1,4-diol	60
13.	β -terpenyl acetate	Ac ₂ O + AcOH	8(9)-p-menth-4-ol-1-yl acetate 3,8(9)-p-menthadiene-1- yl-acetate	61
14.	Dihydro- carveol	tert. butanol	8(9)-p-menthen-2,10-diol 8(9)-p-menthen-2-ol-10-al Dihydrocarvone in traces	17
15.	Dihydro carvyl acetate	tert. butanol	Trans-8(9)-p-menthene-4- ol-2-yl acetate 8(9)-p-menthene-10-al-2- yl-acetate 3,8(9)-p-menthadien-2- yl-acetate	17
16.	β -cedrene	Ac ₂ O + AcOH	Trans β -cedranol	62
17.	Terpinolene (p-menth-1,4 (8) diene)	Ethanol	p-cymene 1-methyl-4-isopropenyl benzene 4-isopropenyl benzyl alcohol	63

No.	Compound	Solvent	Product of oxidation	Reference
18.	Isopulegol (8(9)-p-menth- ene-3-ol)	Tert. butanol	8(9)-p-menthene-3,4-diol 8(9)-p-menthene-3-ol- 10-al.	51
19.	Isopulegyl acetate (8(9)-p-menthene 3-yl-acetate)	Tert. butanol	8(9)-p-menthene-3- acetoxy-4-ol 8(9)-p-menthene-3- acetoxy-10-al	51

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P A R T I I

PREPARATION AND OXIDATION OF SOME
TERPENOIDS WITH SELENIUM DIOXIDE

* * *

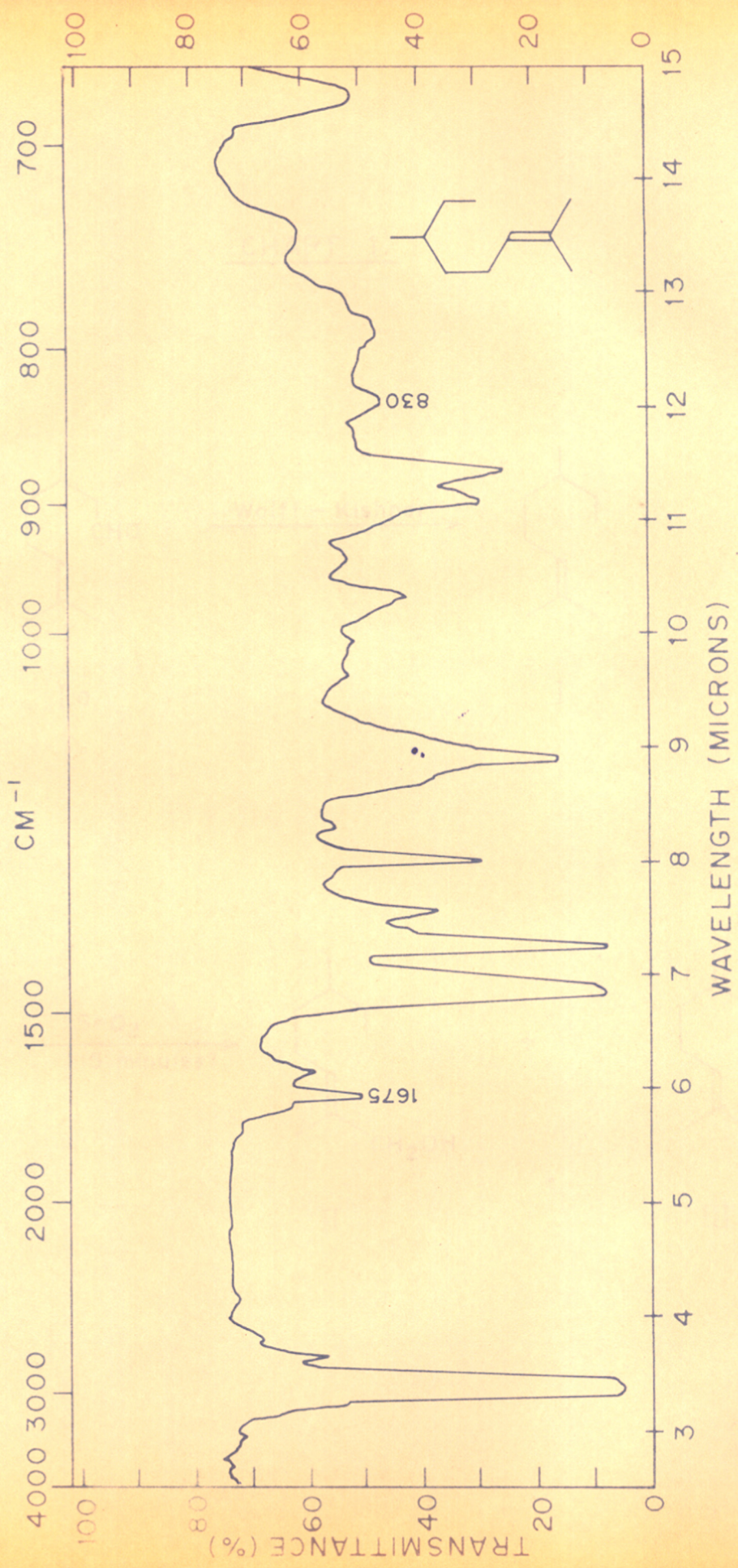
In the introduction, the objective and scope of the work have been discussed. In order to avoid repetition these are not being mentioned again. The work on the preparation and selenium dioxide oxidation of four hydrocarbons is presented below.

2,6-Dimethyl octene-2

This hydrocarbon was prepared¹ from citronellal. Citronellal was distilled and purified through its bisulphite derivative from which pure citronellal was regenerated by treatment with a solution of sodium carbonate. Purified citronellal (Ia) was then subjected to Wolff-Kishner reduction and the hydrocarbon 2,6-dimethyl octene-2 (I) was obtained. It was purified by column chromatography. The purified hydrocarbon gave a single peak in vapour phase chromatography (VPC). Its infrared spectrum (IR-1) showed absorption at 1675 and 830 cm^{-1} indicating the presence of a trisubstituted double bond. The microanalysis results were in conformity with the expected molecular formula $\text{C}_{10}\text{H}_{20}$.

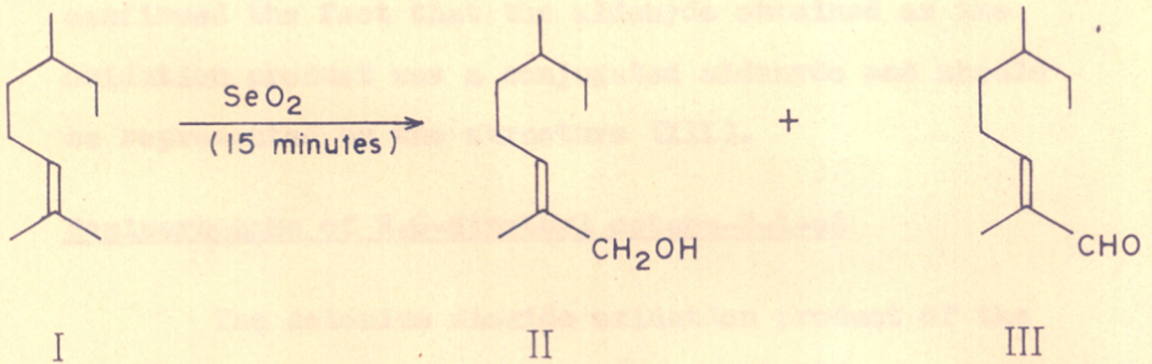
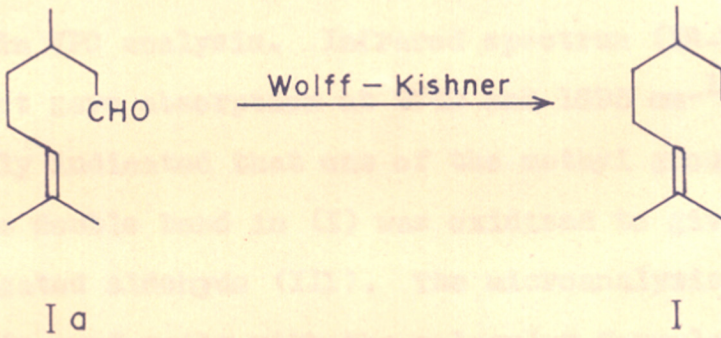
2,6-Dimethyl octene-2-1-al

The hydrocarbon 2,6-dimethyl octene-2 (I) has a trisubstituted double bond which acts as an active centre. When this hydrocarbon was subjected to the action of selenium dioxide, it was expected that following the rules enunciated by Guillemonat,² the substituent α to the more substituted end of the double



IR-1

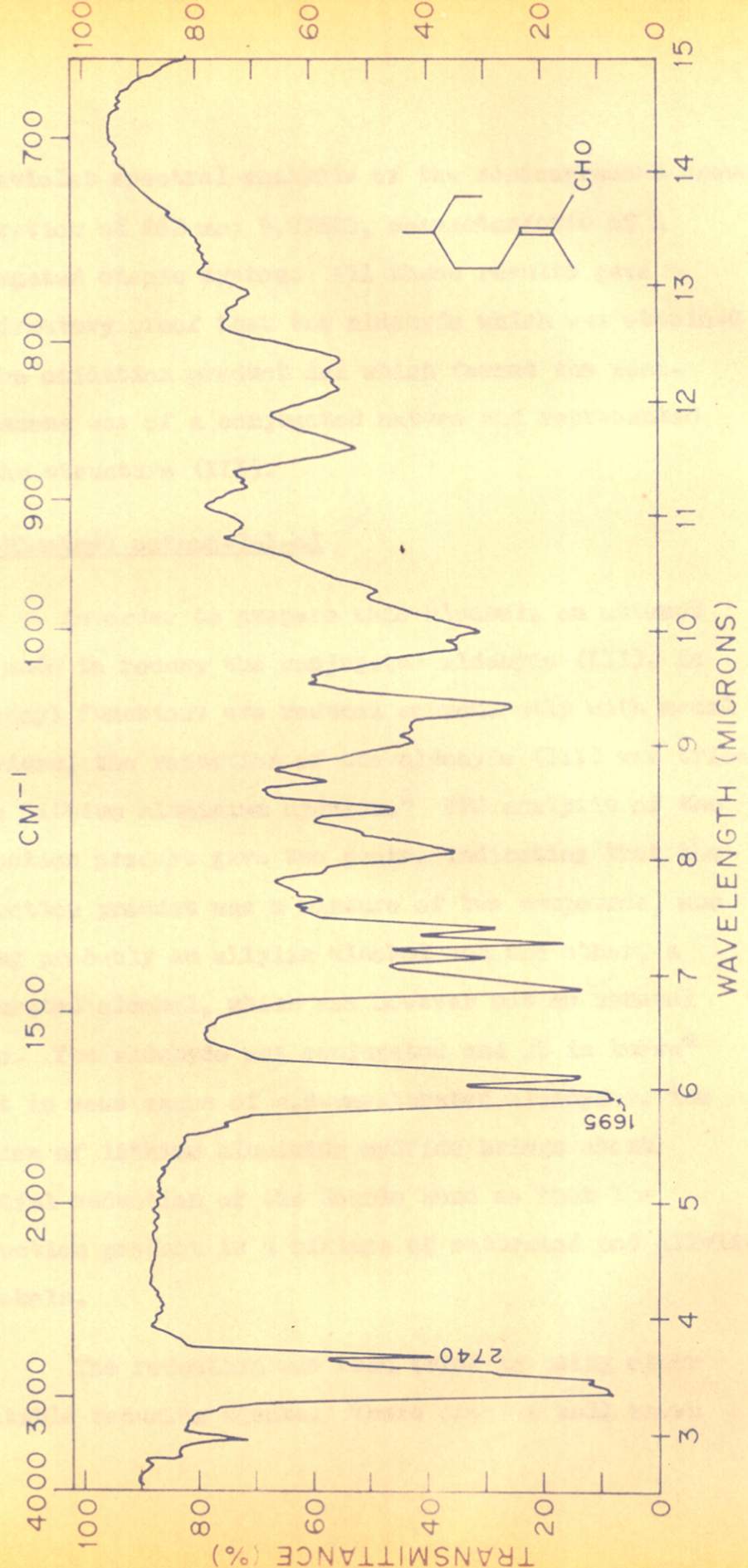
CHART 1.



bond would be oxidised. There are two identical methyl groups attached to the double bond and one of these would be oxidised, thereby giving the allylic alcohol (II) or the conjugated aldehyde (III). After carrying out the reaction for one hour and working up the reaction mixture, the oxidation product gave a single peak in VPC analysis. Infrared spectrum (IR-2) of the product gave absorption at 2740 and 1695 cm^{-1} . This clearly indicated that one of the methyl groups adjacent to the double bond in (I) was oxidised to give the conjugated aldehyde (III). The microanalysis results were in conformity with the molecular formula of the mono-aldehyde $\text{C}_{10}\text{H}_{18}\text{O}$. A further proof as regards the nature of the oxidation product came from the ultraviolet spectrum which showed an absorption at 228.5 $\text{m}\mu$, ϵ , 13900. These results of the ultraviolet spectral analysis confirmed the fact that the aldehyde obtained as the oxidation product was a conjugated aldehyde and should be represented by the structure (III).

Semicarbazone of 2,6-dimethyl octene-2-1-al

The selenium dioxide oxidation product of the hydrocarbon gave a characteristic crystalline semicarbazone, $\text{C}_{11}\text{H}_{21}\text{ON}_3$. Its nitrogen value from microanalytical results indicated that it was a monosemicarbazone. The



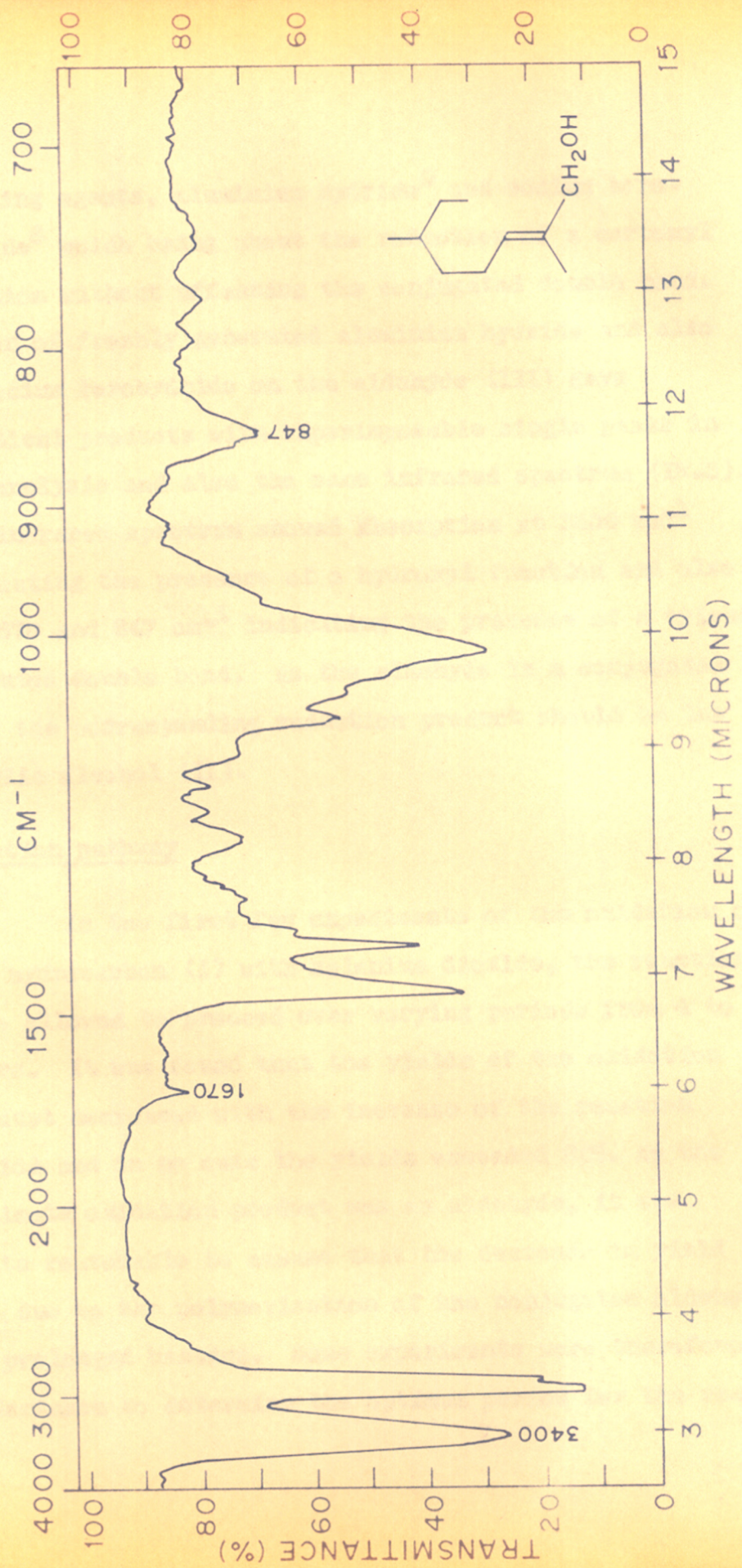
IR - 2

ultraviolet spectral analysis of the semicarbazone showed absorption at $263 \text{ m}\mu$; $\epsilon, 27520$, characteristic of a conjugated dienic system. All these results gave confirmatory proof that the aldehyde which was obtained as the oxidation product and which formed the semicarbazone was of a conjugated nature and represented by the structure (III).

2,6-Dimethyl octene-2-1-ol

In order to prepare this alcohol, an attempt was made to reduce the conjugated aldehyde (III). As carbonyl functions are reduced conveniently with metal hydrides, the reduction of the aldehyde (III) was tried with lithium aluminium hydride.³ VPC analysis of the reduction product gave two peaks, indicating that the reduction product was a mixture of two compounds, one being probably an allylic alcohol and the other, a saturated alcohol, which was however not an unusual case. The aldehyde was conjugated and it is known⁴ that in some cases of α, β -unsaturated aldehydes, the action of lithium aluminium hydride brings about partial reduction of the double bond so that the reduction product is a mixture of saturated and allylic alcohols.

The reduction was then tried by using other suitable reducing agents. There are two well known

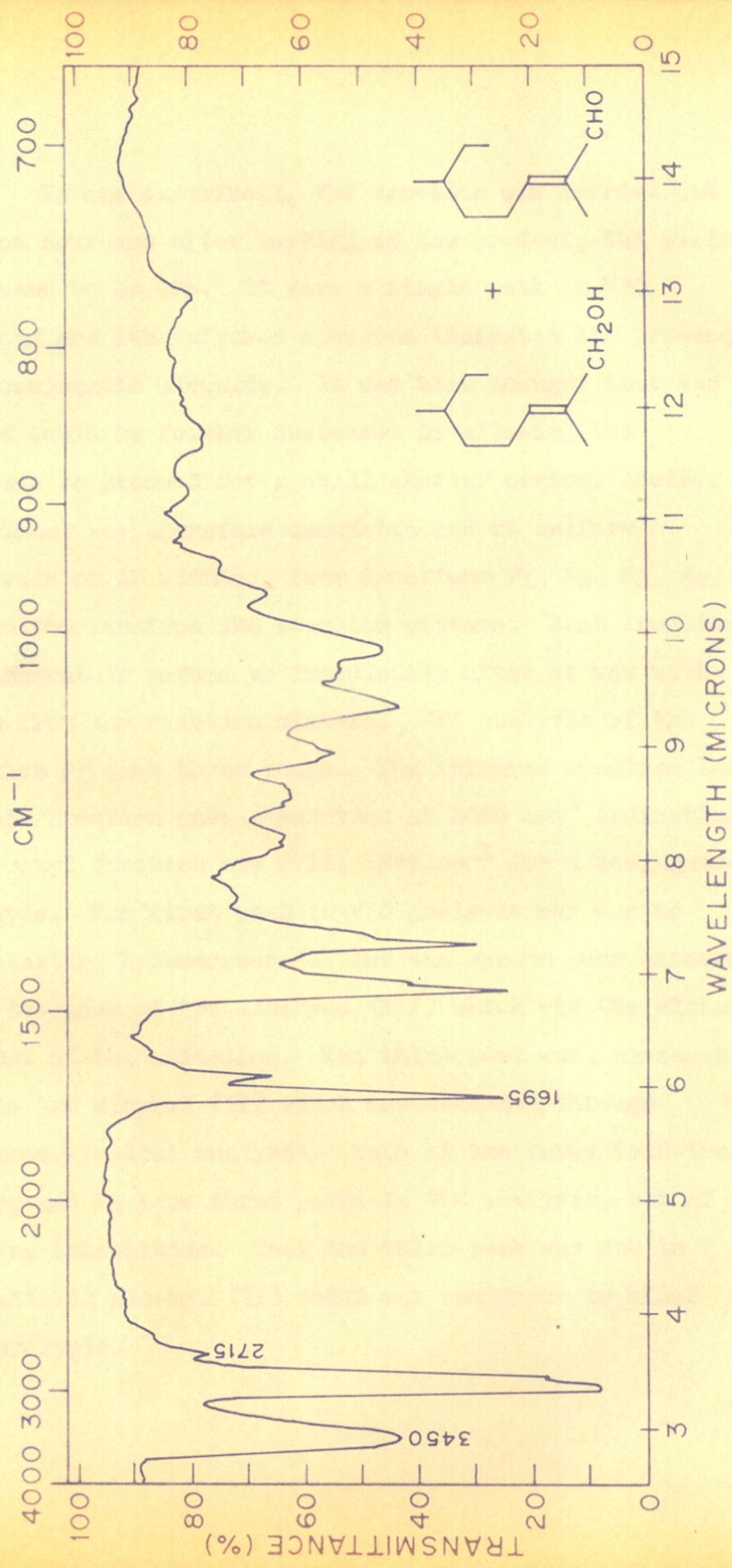


IR-3

reducing agents, aluminium hydride⁵ and sodium borohydride⁶ which bring about the reduction of a carbonyl function without affecting the conjugated double bond. Action of freshly generated aluminium hydride and also of sodium borohydride on the aldehyde (III) gave identical products with superimposable single peaks in VPC analysis and also the same infrared spectrum (IR-3). The infrared spectrum showed absorption at 3400 cm^{-1} indicating the presence of a hydroxyl function and also at 1670 and 847 cm^{-1} indicating the presence of a trisubstituted double bond. As the aldehyde is a conjugated one, the corresponding reduction product should be the allylic alcohol (II).

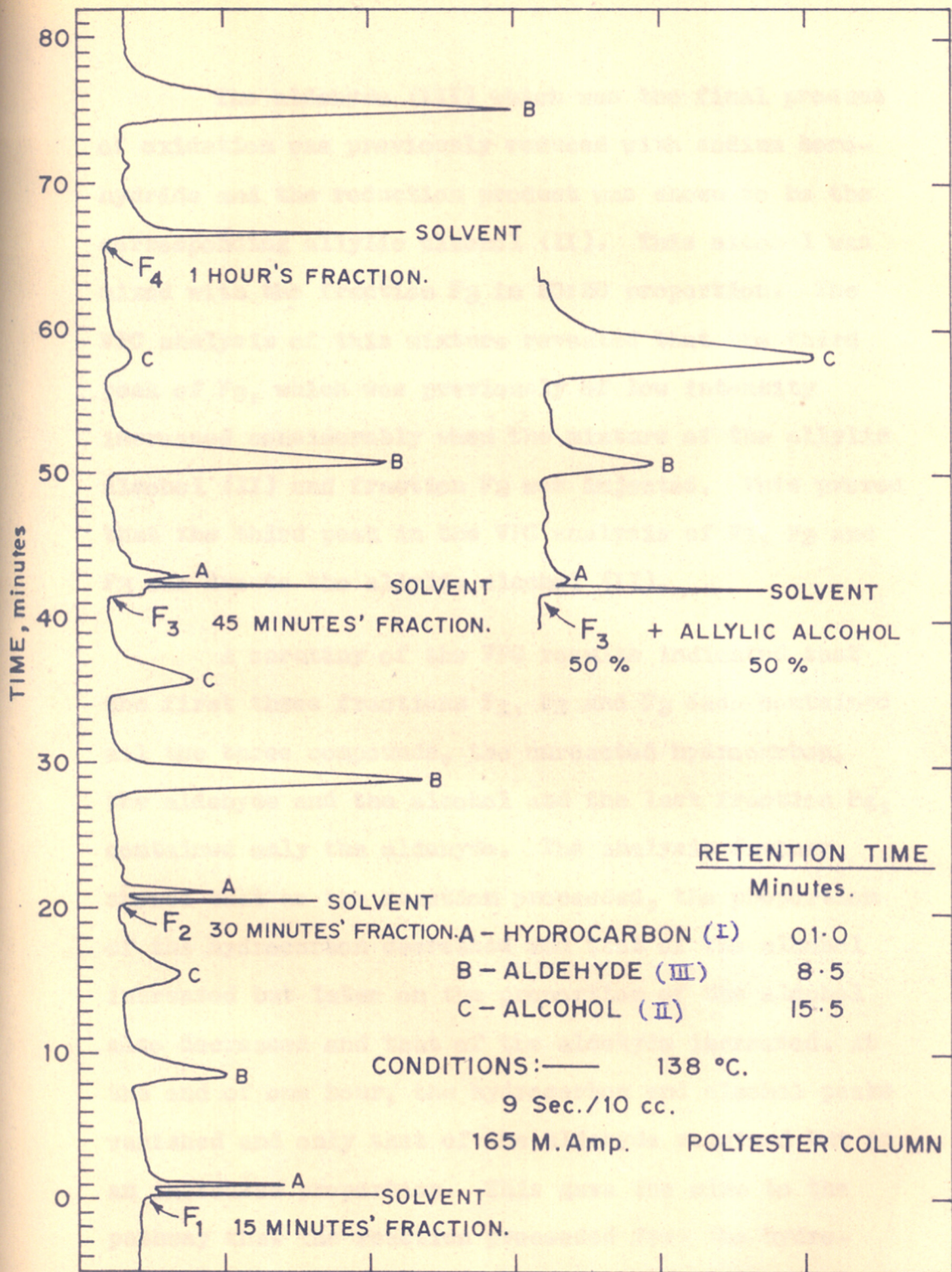
Reaction pathway

In the first few experiments of the oxidation of the hydrocarbon (I) with selenium dioxide, the reactions were allowed to proceed over varying periods from 4 to 8 hours. It was found that the yields of the oxidation product decreased with the increase of the reaction period and in no case the yields exceeded 25%. As the ultimate oxidation product was an aldehyde, it was quite reasonable to assume that the decrease in yield was due to the polymerisation of the conjugated aldehyde by prolonged heating. Some experiments were therefore undertaken to determine the optimum period for the reaction.



IR-4

In one experiment, the reaction was carried out for one hour and after working up the product, the yield was found to be 40%. It gave a single peak in VPC analysis and its infrared spectrum indicated the presence of a conjugated aldehyde. It was then thought that the yields could be further increased by allowing the reaction to proceed for a still shorter period. Another experiment was therefore conducted and at uniform intervals of 15 minutes, four fractions F₁, F₂, F₃, F₄, were withdrawn from the reaction mixture. Each fraction was separately worked up immediately after it was withdrawn from the reaction mixture. VPC analysis of the Fraction F₁ gave three peaks. The infrared spectrum (IR-4) of this fraction gave absorption at 3450 cm⁻¹ indicating a hydroxyl function and 2715, 1695 cm⁻¹ for a conjugated aldehyde. The first peak in VPC analysis was due to the starting hydrocarbon (I) and the second peak concurred with the peak of the aldehyde (III) which was the ultimate product of the oxidation. The third peak was, presumably due to the alcohol (II) which was detected through infrared spectral analysis. Each of the three fractions F₁, F₂ and F₃ gave three peaks in VPC analysis, but of varying intensities. That the third peak was due to the allylic alcohol (II) ~~was~~ was confirmed by mixed VPC analysis.



VPC CHART. OXIDATION OF HYDROCARBON (I).

The aldehyde (III) which was the final product of oxidation was previously reduced with sodium borohydride and the reduction product was shown to be the corresponding allylic alcohol (II). This alcohol was mixed with the fraction F₃ in 50:50 proportion. The VPC analysis of this mixture revealed that the third peak of F₃, which was previously of low intensity increased considerably when the mixture of the allylic alcohol (II) and fraction F₃ was injected. This proved that the third peak in the VPC analysis of F₁, F₂ and F₃ was due to the allylic alcohol (II).

A scrutiny of the VPC results indicated that the first three fractions F₁, F₂ and F₃ each contained all the three compounds, the unreacted hydrocarbon, the aldehyde and the alcohol and the last fraction F₄, contained only the aldehyde. The analysis further showed that as the reaction proceeded, the proportion of the hydrocarbon decreased and that of the alcohol increased but later on the proportion of the alcohol also decreased and that of the aldehyde increased. At the end of one hour, the hydrocarbon and alcohol peaks vanished and only that of the aldehyde remained but in an increased proportion. This gave the clue to the pathway that the reaction proceeded from the hydrocarbon to the conjugated aldehyde via the formation of the allylic alcohol as an intermediate.

α -Santalene

The hydrocarbon fraction of sandalwood oil mainly consists of α -santalene and β -santalene.

α -Santalene (IV) that was previously separated in this laboratory was further purified by repeated chromatography over alumina. Its infrared spectrum (IR-5) showed absorptions at 3050, 1039 cm^{-1} (cyclopropane system), 1660 and 825 cm^{-1} (trisubstituted double bond).

α -Santalol and α -santalal

The hydrocarbon α -santalene (IV) contains a cyclopropane system which is liable to rupture in acidic medium. It was therefore necessary to see that no acidic medium was used in the oxidation of α -santalene. α -Santalene is a tricyclic sesquiterpene with a double bond in the side chain. As the double bond is trisubstituted with two methyl substituents in α - and α' positions, it was expected that by the action of selenium dioxide, one of the methyl substituents would be oxidised to give the allylic alcohol, α -santalol (V) or the conjugated aldehyde, α -santalal (VI).

The oxidation was actually carried out for 4 hours and the oxidation product worked up. The infrared spectrum (IR-6) of the product gave characteristic absorptions at 3400 cm^{-1} indicating the presence of a hydroxyl function,

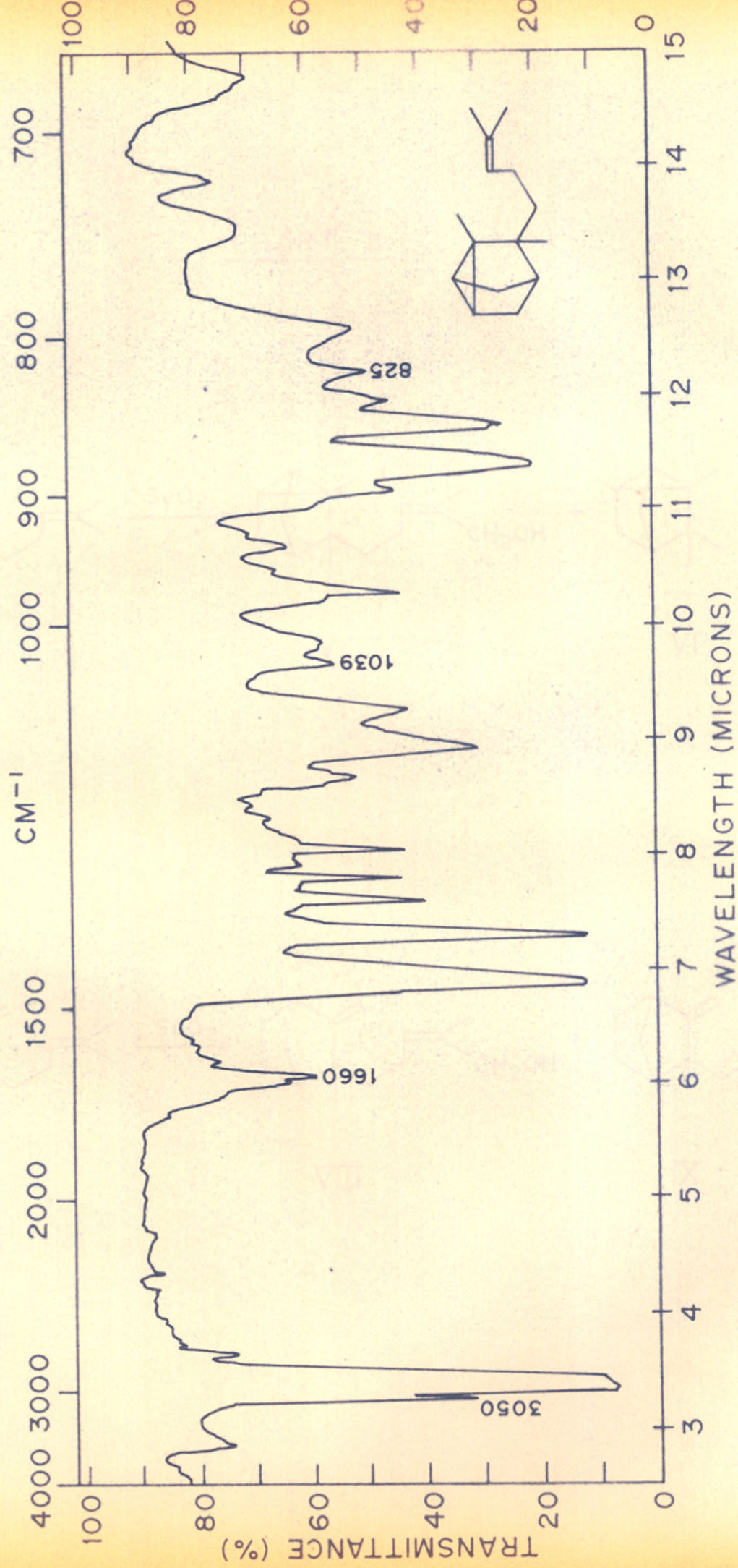
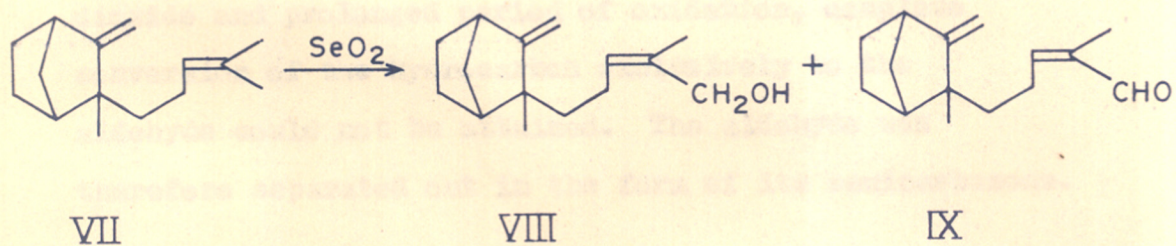
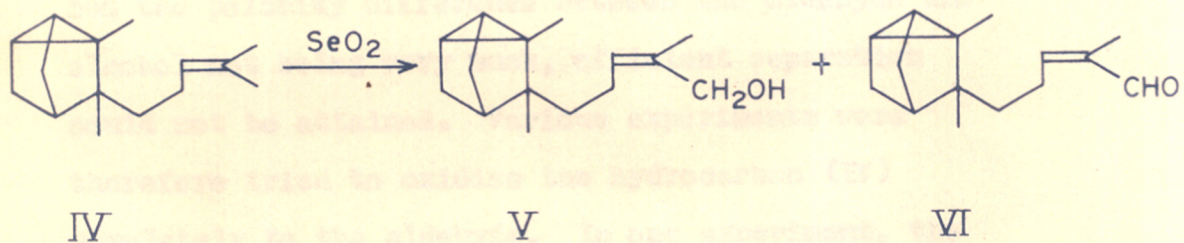


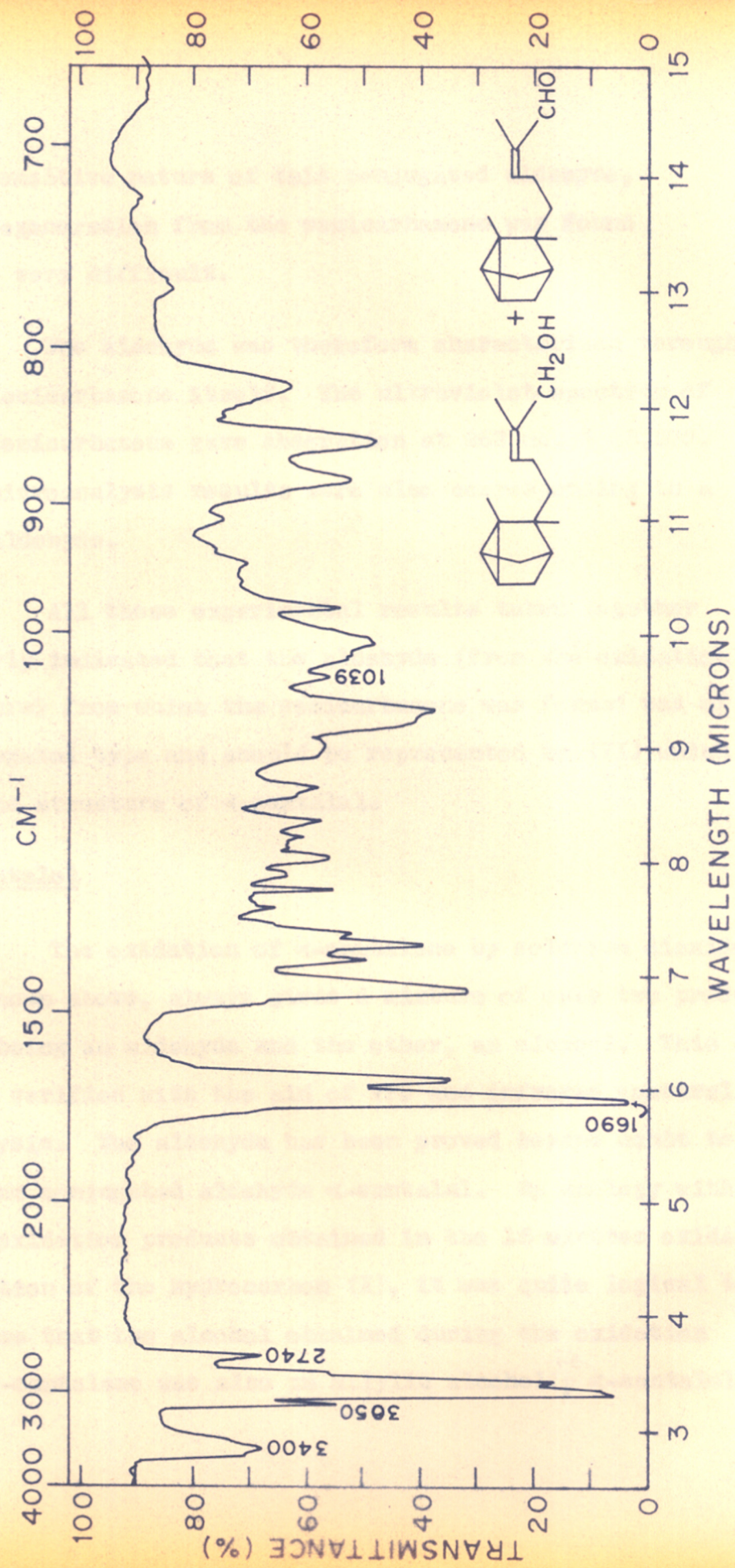
CHART 2.



3050, 1039 cm^{-1} , indicating the cyclopropane system; and 2740, 1690 cm^{-1} indicating the presence of a conjugated aldehyde. VPC analysis also gave two prominent peaks, one corresponding to the aldehyde and the other to the alcohol. Separation of the aldehyde from the alcohol was tried on alumina column, but the polarity difference between the aldehyde and alcohol not being very much, efficient separation could not be attained. Various experiments were therefore tried to oxidise the hydrocarbon (IV) completely to the aldehyde. In one experiment, the oxidation was carried out with a large excess of selenium dioxide and the reaction was allowed to proceed for 10 hours. But even then, the oxidation product was found to contain a substantial proportion of the alcohol. In all these experiments, it was invariably found that inspite of high proportion of selenium dioxide and prolonged period of oxidation, complete conversion of the hydrocarbon exclusively to the aldehyde could not be attained. The aldehyde was therefore separated out in the form of its semicarbazone.

Semicarbazone of α -santalal

From the mixture of the aldehyde and alcohol, obtained as above, the aldehyde was separated out as its crystalline semicarbazone, $\text{C}_{16}\text{H}_{25}\text{ON}_3$. Because of



IR-6

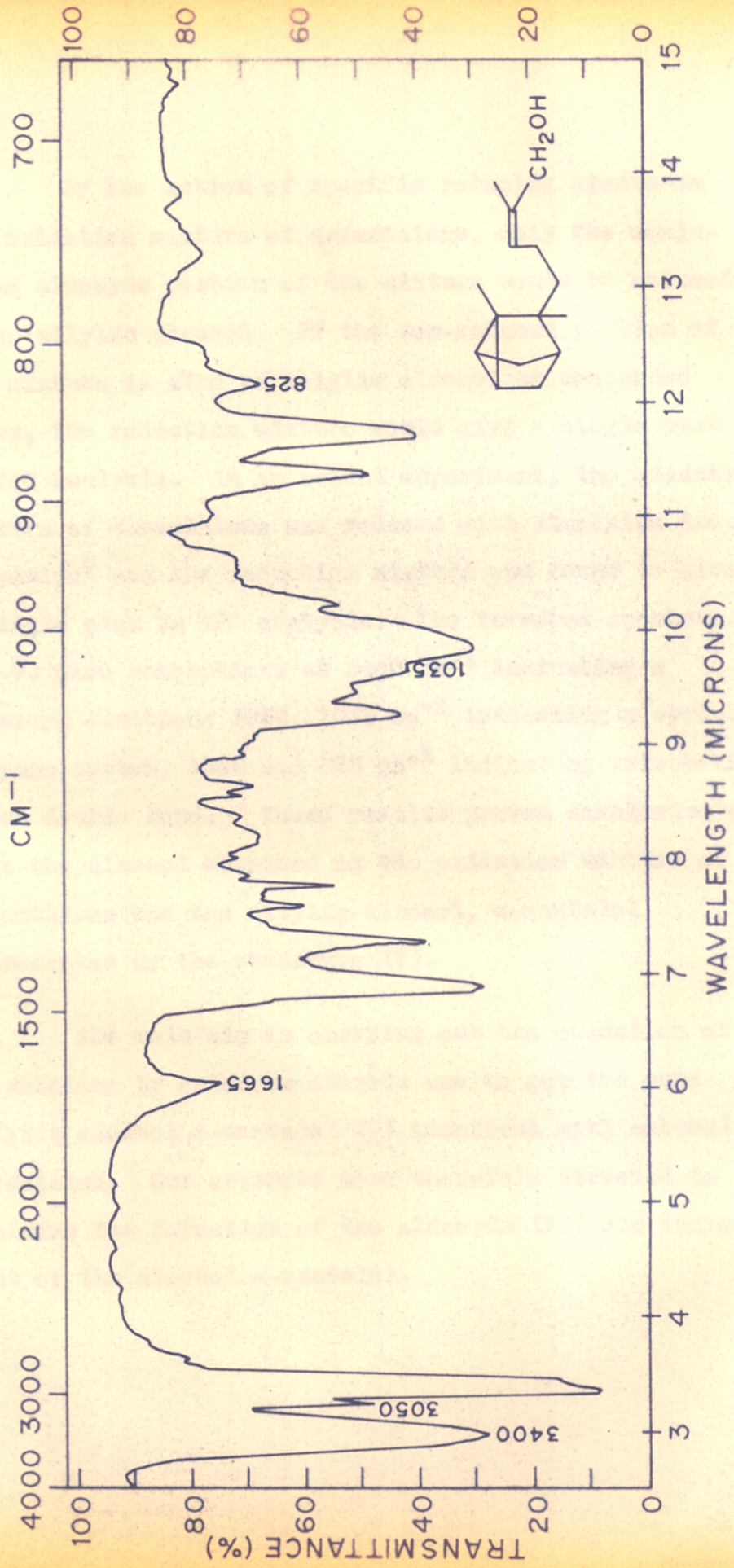
the sensitive nature of this conjugated aldehyde, its regeneration from the semicarbazone was found to be very difficult.

The aldehyde was therefore characterised through the semicarbazone itself. The ultraviolet spectrum of the semicarbazone gave absorption at $262 \text{ m}\mu$, ϵ , 35,570. The microanalysis results were also corresponding to a monoaldehyde.

All these experimental results taken together clearly indicated that the aldehyde (from the oxidation mixture) from which the semicarbazone was formed was of conjugated type and should be represented by (VI) which is the structure of α -santalal.

α -Santalol

The oxidation of α -santalene by selenium dioxide, as shown above, always gives a mixture of only two products, one being an aldehyde and the other, an alcohol. This has been verified with the aid of VPC and infrared spectral analysis. The aldehyde has been proved beyond doubt to be the conjugated aldehyde α -santalal. By analogy with the oxidation products obtained in the 15 minutes oxidation reaction of the hydrocarbon (I), it was quite logical to assume that the alcohol obtained during the oxidation of α -santalene was also an allylic alcohol ^{i.e.} α -santalol.



IR-7

By the action of specific reducing agents on the oxidation mixture of α -santalene, only the conjugated aldehyde portion of the mixture would be reduced to an allylic alcohol. If the non-reduced portion of the mixture is also an allylic alcohol as contended by us, the reduction mixture would give a single peak in VPC analysis. In an actual experiment, the oxidation mixture of α -santalene was reduced with aluminium isopropoxide⁷ and the reduction mixture was found to give a single peak in VPC analysis. The infrared spectrum (IR-7) gave absorptions at 3400 cm^{-1} indicating a hydroxyl function; $3050, 1035\text{ cm}^{-1}$ indicating a cyclopropane system; 1665 and 825 cm^{-1} indicating trisubstituted double bond. These results proved conclusively that the alcohol obtained in the oxidation mixture of α -santalene was the allylic alcohol, α -santalol represented by the structure (V).

The main aim in carrying out the oxidation of α -santalene by selenium dioxide was to get the pure allylic alcohol α -santalol (V) identical with natural α -santalol. Our attempts were therefore directed to minimise the formation of the aldehyde (VI) and increase that of the alcohol α -santalol.

Theoretically one molecule of α -santalene requires one molecule of selenium dioxide to reach the aldehyde stage and as the formation of the aldehyde proceeds through the formation of the intermediate alcohol, only half a molecule of selenium dioxide would be required to oxidise one molecule of α -santalene to α -santalol.

An experiment was therefore conducted wherein selenium dioxide and α -santalene were used in the molecular proportion 1:2. In addition, high dilution technique was used to prevent the concentration of selenium dioxide being too much at any point in the reaction mixture. Selenium dioxide was dissolved in large excess of ethanol and this solution was added drop by drop to a concentrated solution of α -santalene in ethanol under reflux conditions. This high dilution technique was expected to minimise the formation of the aldehyde and arrest the reaction at the alcohol stage. It was however found that the formation of the aldehyde could not be minimised, but on the contrary, a larger proportion of the hydrocarbon remained unreacted. This showed that selenium dioxide oxidised the intermediate alcohol to aldehyde more readily than the hydrocarbon to the intermediate alcohol.

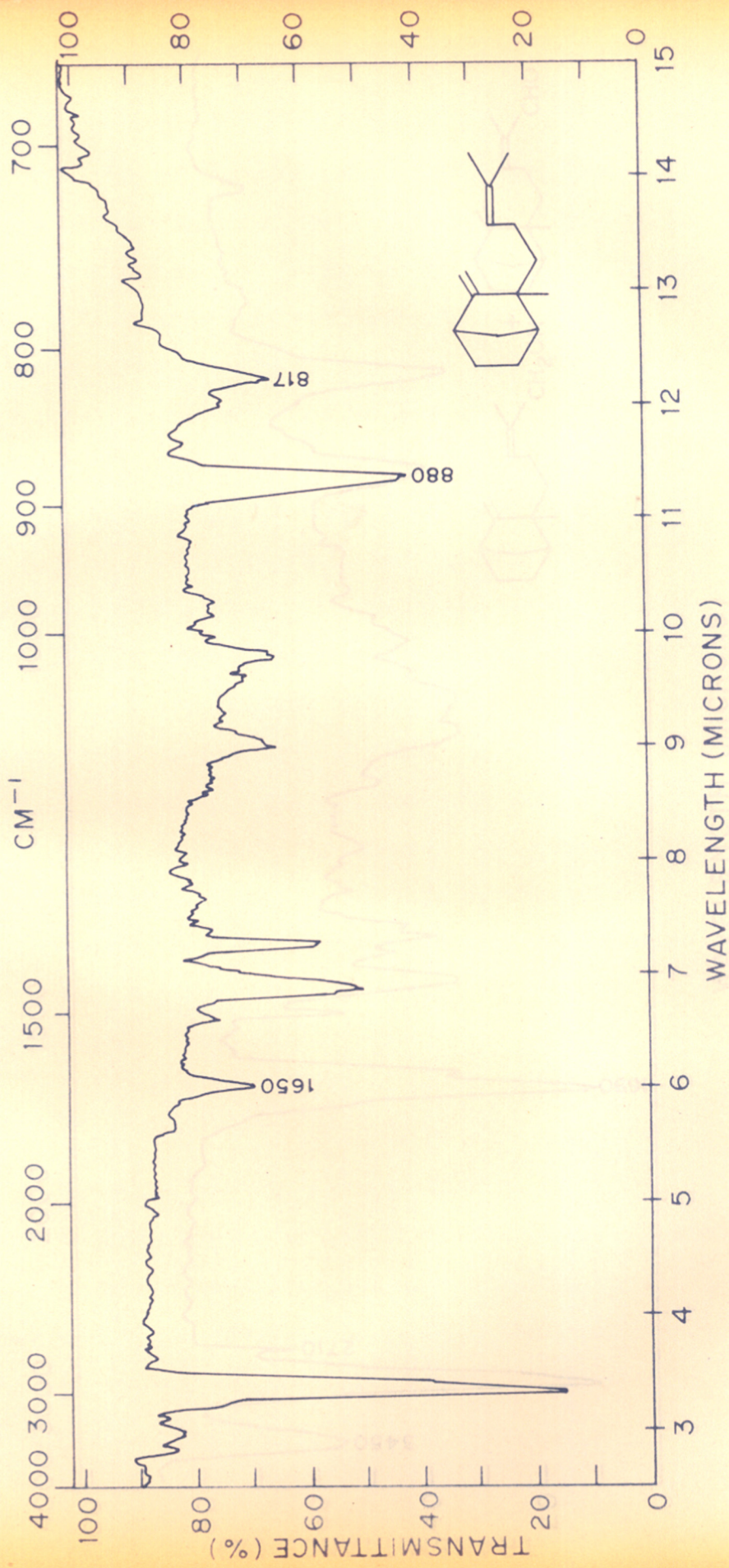
β -Santalene

As in the case of α -santalene, the hydrocarbon β -santalene (VII) was also purified by repeated chromatography over alumina. Its VPC analysis gave essentially one major peak; the purity was about 66%. The infrared spectrum (IR-8) of β -santalene showed absorptions at 1650, 880 cm^{-1} for an exomethylene group and 817 cm^{-1} for a trisubstituted double bond.

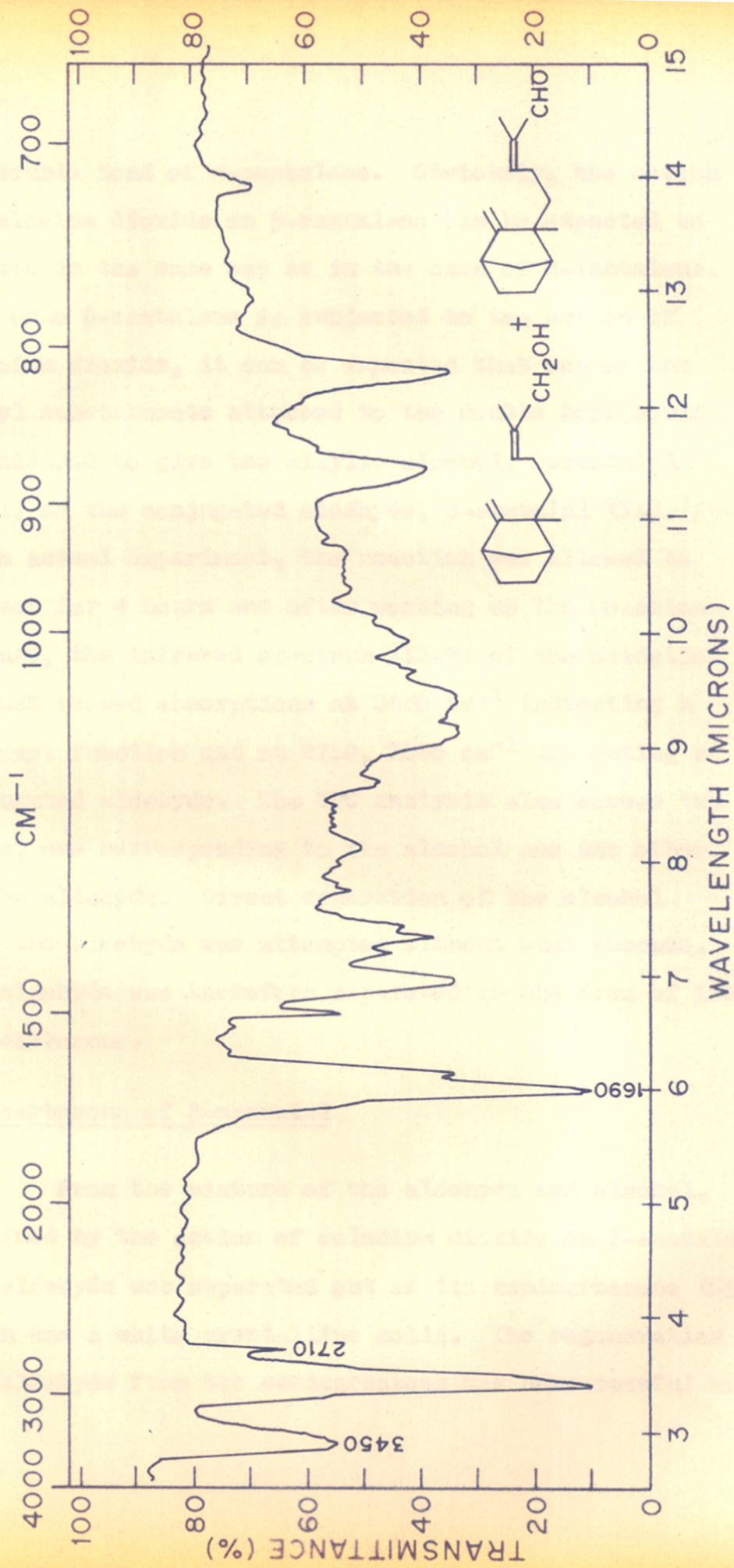
β -Santalol and β -Santalal

β -Santalene is a bicyclic sesquiterpene with two double bonds, one being an exomethylene and the other being a trisubstituted double bond. These two double bonds may be expected to act as active centres in selenium dioxide oxidation. However, in the exomethylene double bond, one of the substituents is a quaternary carbon atom which is not attacked by selenium dioxide. The other substituent is a methine group and as it is at the bridge-head of a ring system, it also cannot be attacked by selenium dioxide. The exomethylene double bond in β -santalene cannot thus have any activating influence in selenium dioxide oxidation reaction.

The other double bond which is trisubstituted and is in the side chain is identical in nature with



IR-8



the double bond of α -santalene. Obviously, the action of selenium dioxide on β -santalene can be expected to proceed in the same way as in the case of α -santalene. Thus when β -santalene is subjected to the action of selenium dioxide, it can be expected that one of the methyl substituents attached to the double bond would be oxidised to give the allylic alcohol, β -santalol (VIII) or the conjugated aldehyde, β -santalal (IX). (Chart-2)

In an actual experiment, the reaction was allowed to proceed for 4 hours and after working up the reaction mixture, the infrared spectrum (IR-9) of the oxidation product showed absorptions at 3450 cm^{-1} indicating a hydroxyl function and at $2710, 1690\text{ cm}^{-1}$ indicating a conjugated aldehyde. The VPC analysis also showed two peaks, one corresponding to the alcohol and the other to the aldehyde. Direct separation of the alcohol from the aldehyde was attempted without much success. The aldehyde was therefore separated in the form of its semicarbazone.

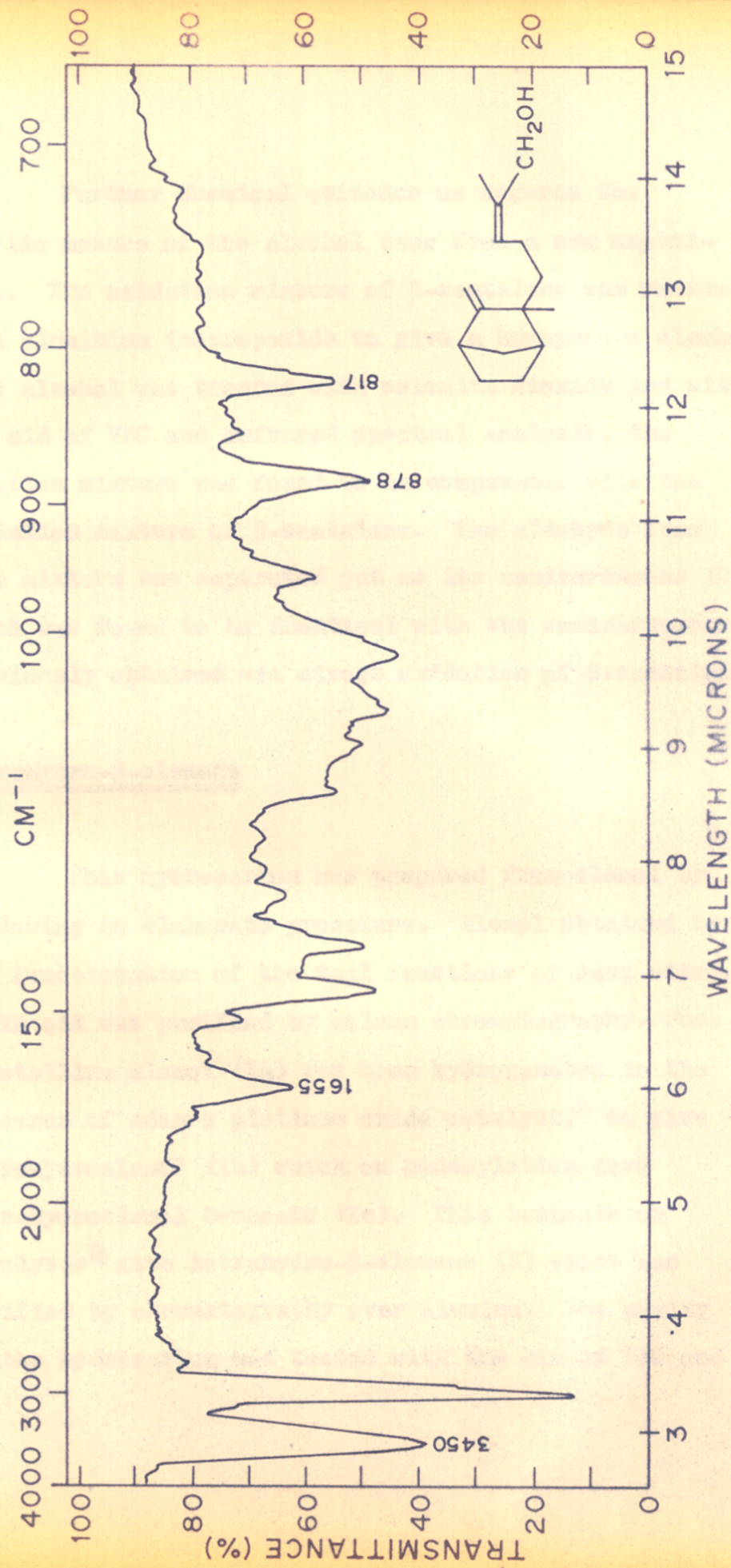
Semicarbazone of β -santalal

From the mixture of the aldehyde and alcohol, obtained by the action of selenium dioxide on β -santalene, the aldehyde was separated out as its semicarbazone (S1) which was a white crystalline solid. The regeneration of the aldehyde from the semicarbazone was unsuccessful and

the aldehyde was therefore characterised through the semicarbazone itself. The ultraviolet spectrum of the semicarbazone gave absorption at $263 \text{ m}\mu$, ϵ , 37010. The microanalysis results were corresponding to a mono-aldehyde. All these evidences taken together indicated that the aldehyde which was present in the oxidation mixture and from which the above semicarbazone was obtained must be the conjugated aldehyde β -santalal represented by the structure (IX).

β -Santalol

The oxidation of β -santalene by selenium dioxide invariably gave a mixture of the aldehyde (IX), and alcohol (VIII). As in the case of α -santalene, here also the reaction could not be arrested at the alcohol stage. The oxidation mixture on reduction with aluminium isopropoxide gave a homogenous alcohol with a single peak in VPC analysis and the infrared spectrum (IR-10) showed absorptions at 3450 cm^{-1} for a hydroxyl function, 1655 , 878 cm^{-1} indicating an exo-methylene group; and 817 cm^{-1} for trisubstituted double bond. Thus the alcohol obtained by reduction of the oxidation mixture and the unreduced alcohol in the oxidation mixture were shown to be one and the same, thereby establishing the fact that the alcohol in the oxidation mixture was the allylic alcohol, β -santalol, represented by (VIII).



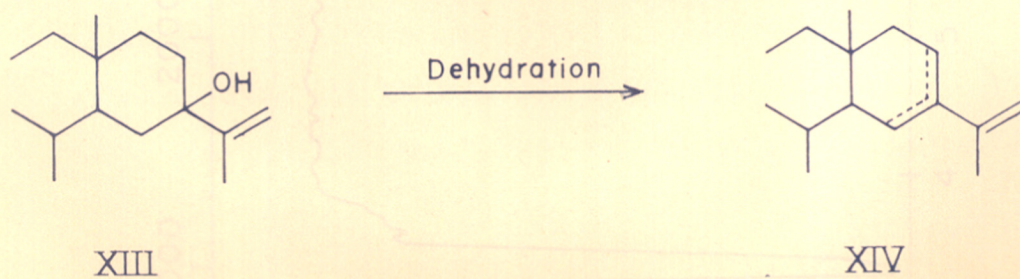
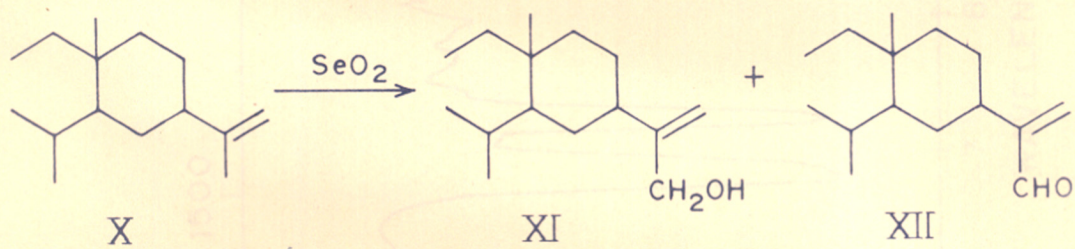
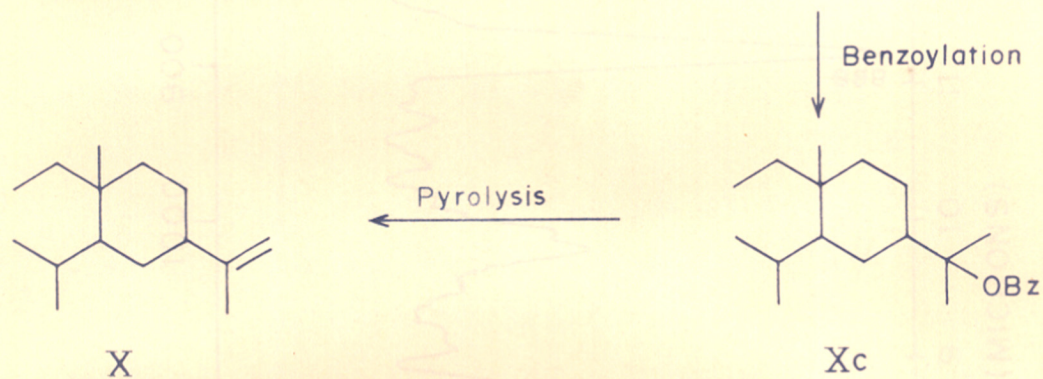
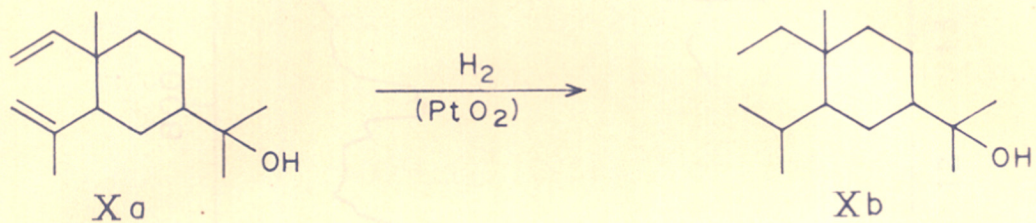
IR-10

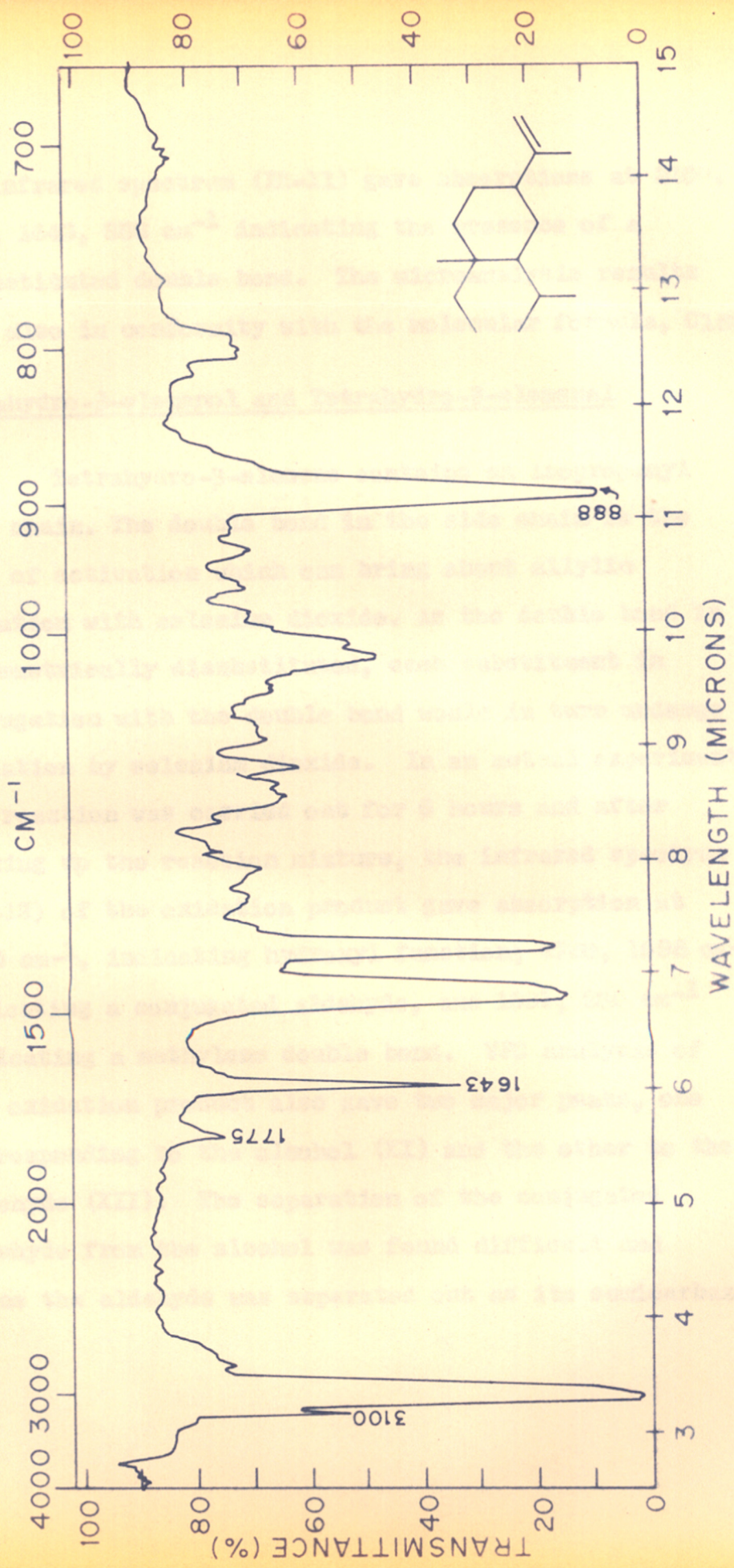
Further chemical evidence as regards the allylic nature of the alcohol came from a new experiment. The oxidation mixture of β -santalene was reduced with aluminium isopropoxide to give a homogenous alcohol. This alcohol was treated with selenium dioxide and with the aid of VPC and infrared spectral analysis, the reaction mixture was found to be comparable with the oxidation mixture of β -santalene. The aldehyde from this mixture was separated out as its semicarbazone (S₂) which was found to be identical with the semicarbazone (S₁) previously obtained via direct oxidation of β -santalene.

Tetrahydro- β -elemene

This hydrocarbon was prepared from elemol by following an elaborate procedure. Elemol obtained by the fractionation of the tail fractions of Java citronella oil was purified by column chromatography. Pure crystalline elemol (Xa) was then hydrogenated in the presence of Adam's platinum oxide catalyst,⁷ to give tetrahydroelemol (Xb) which on benzylation gave tetrahydroelemol benzoate (Xc). This benzoate on pyrolysis⁸ gave tetrahydro- β -elemene (X) which was purified by chromatography over alumina. The purity of the hydrocarbon was tested with the aid of VPC and

CHART 3.



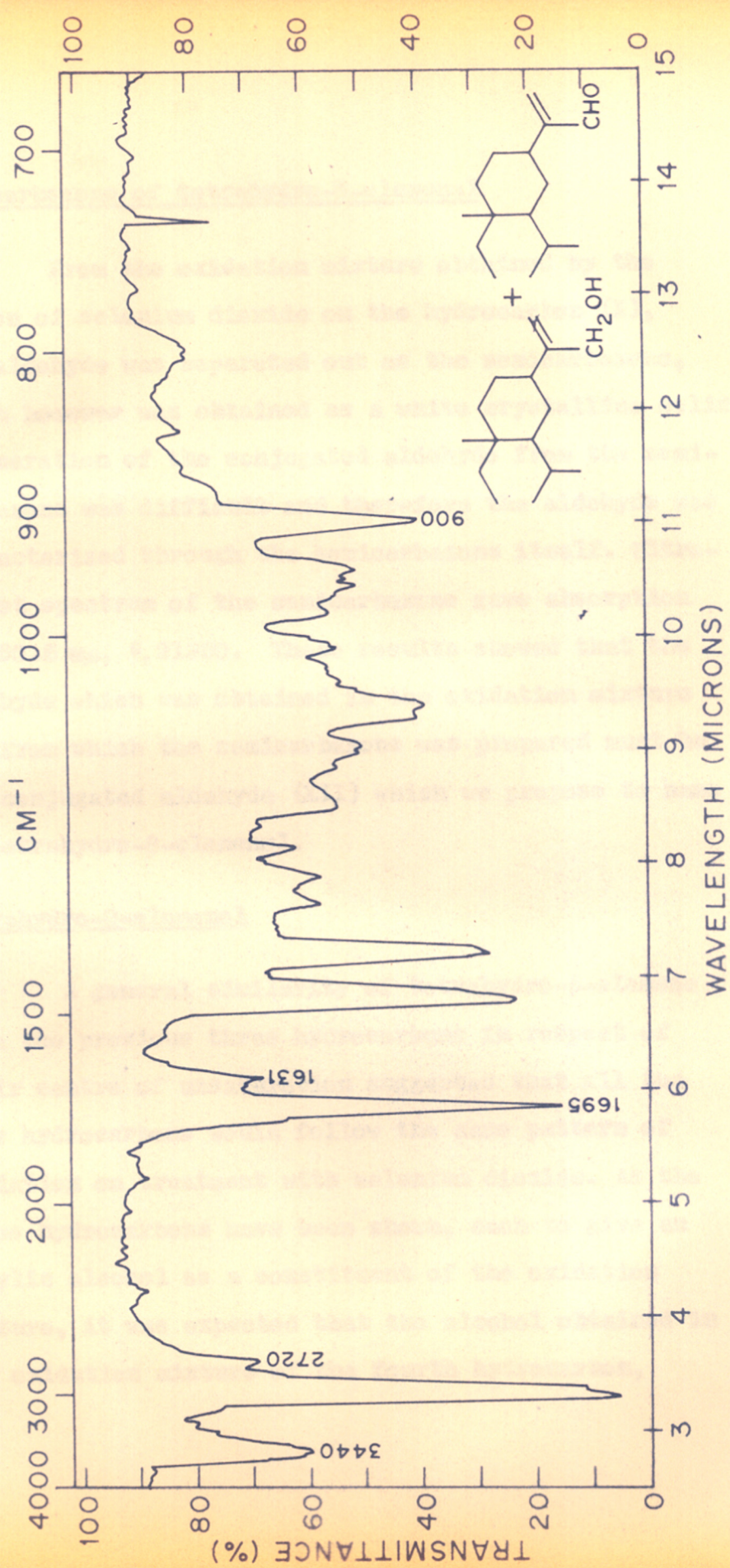


IR-11

its infrared spectrum (IR-11) gave absorptions at 3100, 1775, 1643, 888 cm^{-1} indicating the presence of a disubstituted double bond. The microanalysis results were also in conformity with the molecular formula, $\text{C}_{15}\text{H}_{28}$.

Tetrahydro- β -elemenol and Tetrahydro- β -elemenal

Tetrahydro- β -elemene contains an isopropenyl side chain. The double bond in the side chain is the seat of activation which can bring about allylic oxidation with selenium dioxide. As the double bond is unsymmetrically disubstituted, each substituent in conjugation with the double bond would in turn undergo oxidation by selenium dioxide. In an actual experiment, the reaction was carried out for 6 hours and after working up the reaction mixture, the infrared spectrum (IR-12) of the oxidation product gave absorption at 3440 cm^{-1} , indicating hydroxyl function; 2720, 1695 cm^{-1} , indicating a conjugated aldehyde, and 1631, 900 cm^{-1} indicating a methylene double bond. VPC analysis of the oxidation product also gave two major peaks, one corresponding to the alcohol (XI) and the other to the aldehyde (XII). The separation of the conjugated aldehyde from the alcohol was found difficult and hence the aldehyde was separated out as its semicarbazone.

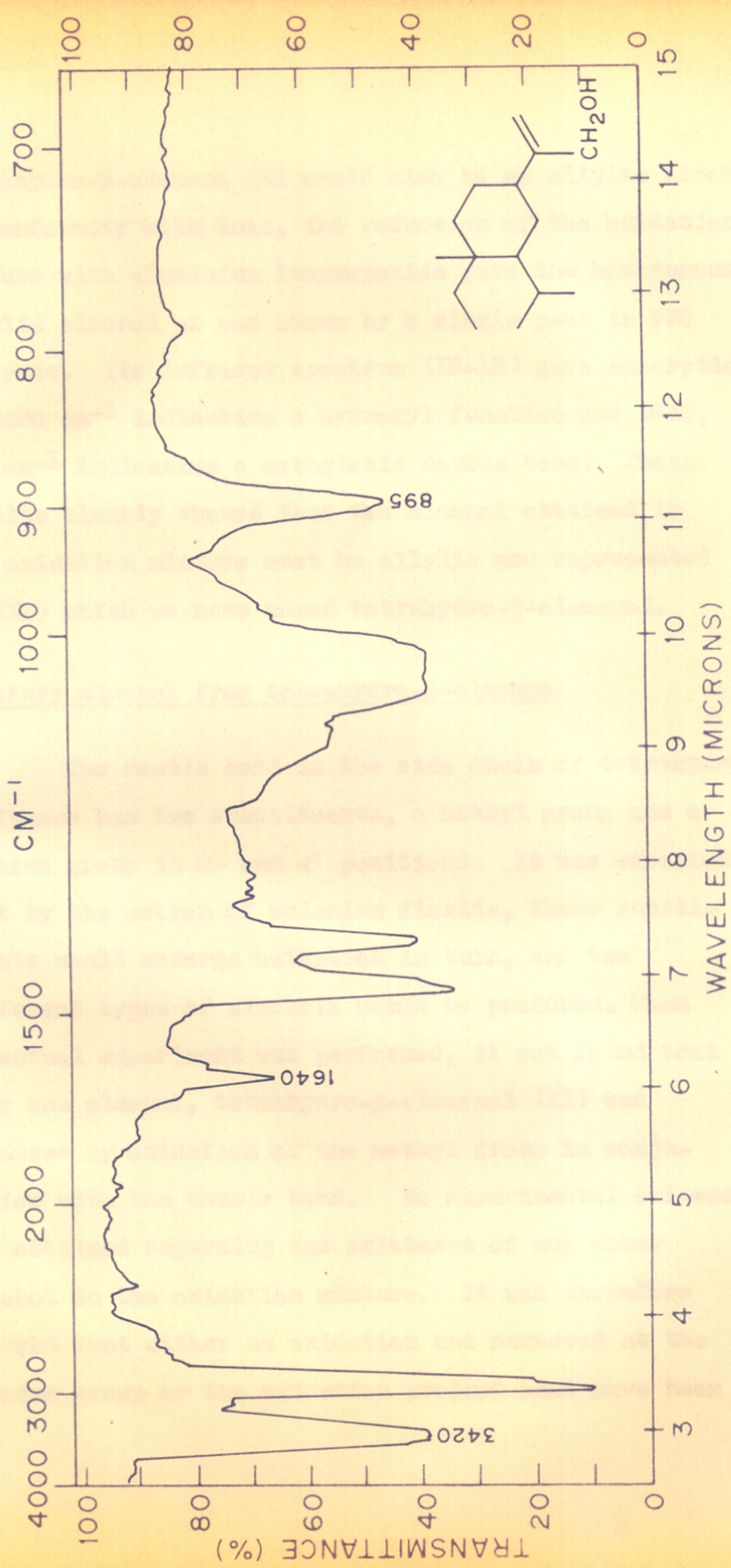


Semicarbazone of tetrahydro- β -elemenal

From the oxidation mixture obtained by the action of selenium dioxide on the hydrocarbon (X), the aldehyde was separated out as the semicarbazone, which ~~however~~ was obtained as a white crystalline solid. Regeneration of the conjugated aldehyde from the semicarbazone was difficult and therefore the aldehyde was characterised through the semicarbazone itself. Ultra-violet spectrum of the semicarbazone gave absorption at 260.5 $m\mu$, ϵ , 21350. These results showed that the aldehyde which was obtained in the oxidation mixture and from which the semicarbazone was prepared must be the conjugated aldehyde (XII) which we propose to name as tetrahydro- β -elemenal.

Tetrahydro- β -elemenol

A general similarity of tetrahydro- β -elemene with the previous three hydrocarbons in respect of their centre of unsaturation suggested that all the four hydrocarbons would follow the same pattern of oxidation on treatment with selenium dioxide. As the three hydrocarbons have been shown, each to give an allylic alcohol as a constituent of the oxidation mixture, it was expected that the alcohol obtained in the oxidation mixture of the fourth hydrocarbon,



IR - 13

tetrahydro- β -elemene (X) would also be an allylic alcohol. In conformity with this, the reduction of the oxidation mixture with aluminium isopropoxide gave the homogenous allylic alcohol as was shown by a single peak in VPC analysis. Its infrared spectrum (IR-13) gave absorptions as 3420 cm^{-1} indicating a hydroxyl function and 1640 , 895 cm^{-1} indicating a methylenic double bond. These results clearly showed that the alcohol obtained in the oxidation mixture must be allylic and represented by (XI) which we have named tetrahydro- β -elemenol.

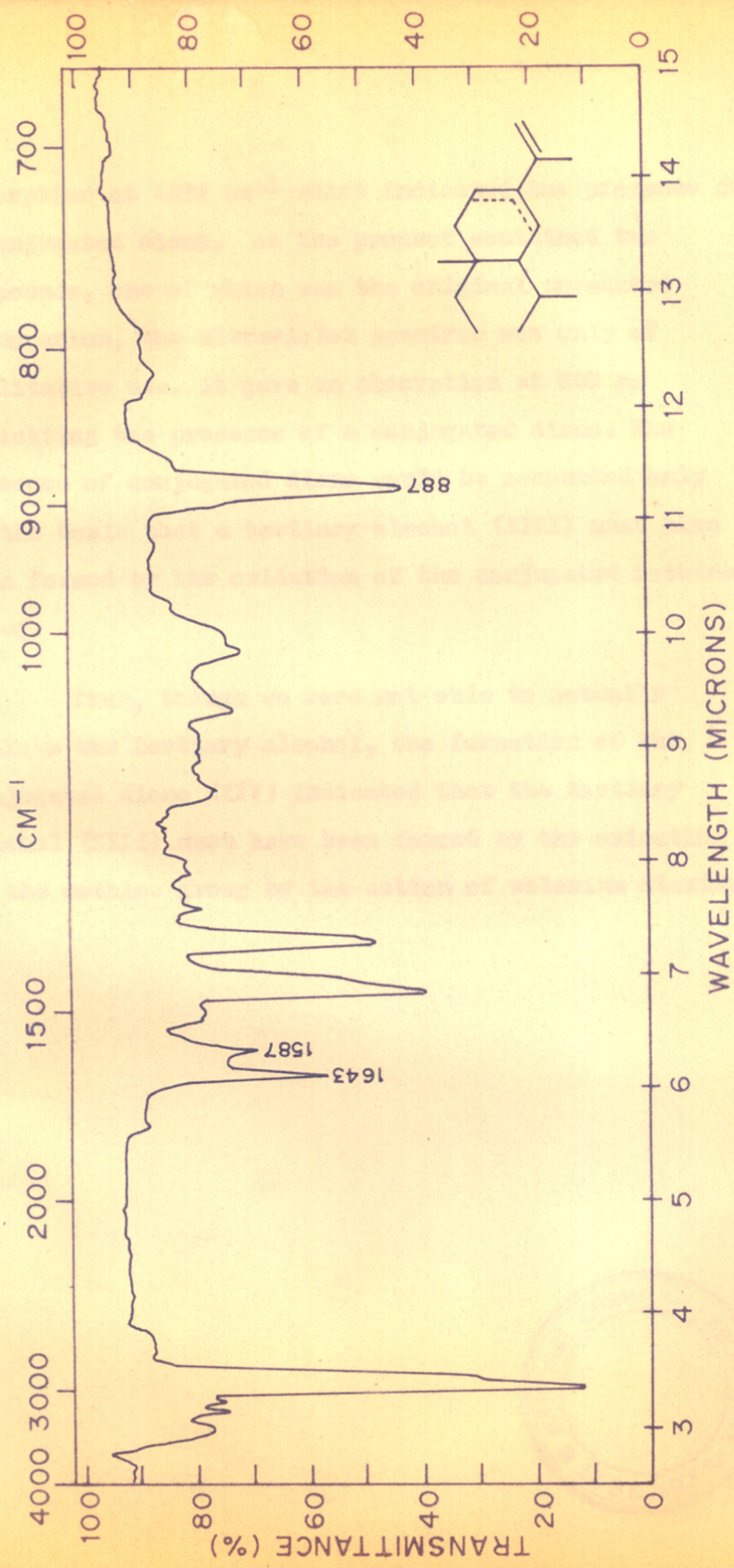
Tertiary alcohol from tetrahydro- β -elemene

The double bond in the side chain of tetrahydro- β -elemene has two substituents, a methyl group and a methine group in α - and α' positions. It was expected that by the action of selenium dioxide, these substituents would undergo oxidation in turn, and two different types of alcohols would be produced. When an actual experiment was performed, it was found that only one alcohol, tetrahydro- β -elemenol (XI) was produced by oxidation of the methyl group in conjugation with the double bond. No experimental evidence was obtained regarding the existence of any other alcohol in the oxidation mixture. It was therefore thought that either no oxidation had occurred at the methine group or the oxidation product must have been

lost at some stage or it must have undergone some transformation.

Theoretically, it is postulated that of the methyl and methine groups in conjugation with the double bond, the methine group is less reactive. This might result in low yield of a tertiary alcohol. The latter may subsequently undergo dehydration due to heating and the conjugated diene formed may be lost due to polymerisation.

Anticipating this, an experiment was conducted wherein the action of selenium dioxide was allowed to proceed for a short period of 3 hours only, so as to minimise the chances of the polymerisation of the conjugated diene that might be formed as explained above. The reaction mixture was worked up as usual and immediately, the oxidation product was chromatographed over alumina grade I, and eluted with pet.ether (40-60°). From the eluent, pet.ether was removed by distillation. The residual product which contained only hydrocarbon gave two peaks in VPC analysis, one corresponding to the original hydrocarbon (X) and one for an unidentified compound. The infrared spectrum (IR-14) showed that besides the absorptions at 1643 and 888 cm^{-1} which were obtained for the starting hydrocarbon, there was another



IR - 14

absorption at 1587 cm^{-1} which indicated the presence of a conjugated diene. As the product contained two compounds, one of which was the original unreacted hydrocarbon, the ultraviolet spectrum was only of qualitative use. It gave an absorption at $232\text{ m}\mu$ indicating the presence of a conjugated diene. The presence of conjugated diene could be accounted only on the basis that a tertiary alcohol (XIII) must have been formed by the oxidation of the conjugated methine group.

Thus, though we were not able to actually isolate the tertiary alcohol, the formation of the conjugated diene (XIV) indicated that the tertiary alcohol (XIII) must have been formed by the oxidation of the methine group by the action of selenium dioxide.



EXPERIMENTAL2,6-Dimethyl octene-2 (I)

This hydrocarbon was obtained from citronellal by Huang-Minlon reaction.

Citronellal supplied by M/s S.H. Kelkar & Co., Bombay, was distilled. The product showed two peaks (VPC), indicating the presence of an impurity. Pure citronellal was obtained from the bisulphite derivatives.

Bisulphite derivative

A saturated solution of sodium sulphite (350 g) in water (1170 ml) was prepared. On addition of a few drops of 1% phenolphthalein solution, it showed a pink colour which was just discharged by dropwise addition of 50% acetic acid. Freshly distilled citronellal (155 g) was added to this solution, and the mixture thoroughly shaken and immersed in a boiling water-bath. The pink colour reappeared but was discharged by adding acetic acid. This process of shaking, heating and adding acetic acid was continued till the pink colour just disappeared at the boiling point of water. After cooling to room temperature, solid bisulphite adduct started separating out. It was filtered, ^{pressed} passed several times,

kneaded

treated with ether in a mortar and filtered when the solid bisulphite adduct (180 g) was obtained.

Regeneration of citronellal (Ia)

Sodium carbonate (106 g) was dissolved in water (535 ml) and to the stirring solution, the bisulphite adduct (180 g) was added in small portions. The solution was covered with pet.ether (60-80°; 300 ml) and refluxed on a water bath for two hours. After cooling, the pet. ether layer was separated out and the aqueous portion was extracted three times with pet.ether (100 ml each time). The combined extract of pet.ether was dried over anhydrous sodium sulphate and filtered, and after removal of the pet.ether, the residue was distilled under reduced pressure when pure citronellal (55 g; VFC single peak) was obtained, b.p. 92°/15 mm., n_D^{27} 1.4450; $(\alpha)_D^{27} + 11.7^\circ$ (c, 10.0).

Infrared spectrum (liquid film):

2725, 1724 cm^{-1} (-CHO), 833 cm^{-1} (trisubstituted double bond).

2,6-Dimethyl-octene-2 (I)

Citronellal was reduced according to Huang-Minlon procedure followed by Eschinazi¹. A mixture of purified citronellal (50 g), hydrazine hydrate (35 ml; 85%), diethylene glycol (300 ml), and potassium hydroxide (55 g) was refluxed at 140° for one hour. Water was distilled

off by raising the temp. to 180° . The distillate was shaken with a saturated solution of sodium chloride and the upper layer of the hydrocarbon was returned to the reaction flask. The reaction mixture was further refluxed at 180° for 3 hours and then it was distilled by raising the temperature to 250° . The distillate was treated with a saturated solution of sodium chloride and the hydrocarbon separating out as an upper layer was removed. It was successively treated with 10% sulphuric acid, water, sodium carbonate solution, water and finally dried over potassium hydroxide. The hydrocarbon was further purified by passing over alumina (neutral, grade I, 1:30) and eluting with pet. ether. From the eluent, pet. ether was removed by distillation on a water bath and the residual portion was the required hydrocarbon which was refluxed over sodium and distilled under vacuum, b.p. $60^{\circ}/15$ mm., n_D^{25} 1.4271; $(n_D^{25})^2 + 9.3^{\circ}$ (clean), VPC single peak.

Analysis

Found: C, 85.92; H, 14.31.

Calc. for $C_{10}H_{20}$: C, 85.72; H, 14.29%.

Infrared spectrum (IR-1):

1675, 830 cm^{-1} (trisubstitution).

2,6-Dimethyl-octene-2-1-al (III)

The hydrocarbon, 2,6-dimethyl-octene-2 (7 g; 0.05 mole) was dissolved in alcohol (25 ml) in a round bottom flask (100 ml) and to this was added a solution of selenium

dioxide (7.8 g) in alcohol (25 ml). The mixture was refluxed on a water bath for one hour. In the beginning the mixture attained a pale yellow colour which, as the reaction progressed, changed to yellow, pale brown and finally deep brown colour. Also with the progress of the reaction, black particles of selenium metalloid started depositing. After refluxing for one hour, the reaction mixture was cooled and filtered through cotton. From the filtrate, the solvent was removed by distillation under vacuum using a water pump. Finally, the product was distilled under vacuum on oil bath. The distillate (2.8 g) was a pale yellow liquid, its infrared spectrum showing the presence of an aldehyde function.

In a second experiment, after refluxing the mixture for one hour, the product was filtered through cotton, diluted with two times its own volume of water and extracted with ether (three times). The combined ether extract was washed with water, dried over anhydrous sodium sulphate and filtered. Ether was removed by distillation and the residue was distilled, under vacuum on oil-bath, when 2,6-dimethyl-octene-2-1-al was obtained; b.p. $70^{\circ}/2$ mm., n_D^{25} 1.4530, $(\alpha)_D^{25} + 9.96^{\circ}$ (clean); VPC single peak.

Analysis

Found: C, 77.21; H, 11.80.

Calc. for $C_{10}H_{18}O$: C, 77.86; H, 11.76%.

Infrared spectrum (IR-2)

2740, 1695 cm^{-1} (conjugated aldehyde).

Ultraviolet spectrum

λ_{max} . 228.5 $m\mu$; ϵ max. 13900.

The aldehyde was unstable and could not be preserved for more than two days even in the cold.

Semicarbazone of the aldehyde

To a solution of semicarbazide hydrochloride (0.5 g) and sodium acetate (0.8 g) in water (4 ml), the aldehyde (0.4 g) was added. A slight turbidity appeared which was discharged by adding alcohol (3 ml). The solution was warmed on water bath for a few minutes and kept aside overnight. The precipitated semicarbazone was filtered and washed with cold water. The crude product was repeatedly crystallised from hot alcohol when pure semicarbazone (0.34 g) was obtained, m.p. 177-178°.

Analysis

Found: N, 20.0.

Calc. for $C_{11}H_{21}ON_3$: N, 19.9%.

Ultraviolet spectrum

λ_{max} . 263 $m\mu$; ϵ max. 27520.

2,6-Dimethyl octene-2-1-ol (II)(a) Reduction of the aldehyde with aluminium hydride

Freshly generated aluminium hydride obtained by interaction between LAH and anhydrous $AlCl_3$ was used for the reduction of the aldehyde 2,6-dimethyl octene-2-1-al.

In a two necked conical flask fitted with a condenser (calcium chloride tube) and a dropping funnel (calcium chloride tube) dry ether (100 ml), $LiAlH_4$ (0.45 g) and anhydrous aluminium chloride (0.55 g) were taken and the mixture was kept stirring (magnetic stirrer). The stirring was continued till the grey colour of $LiAlH_4$ gradually disappeared and white foam-like layer was formed indicating the generation of AlH_3 .

A solution of the aldehyde (0.7 g) in dry ether (10 ml) was added from the dropping funnel to the ice-cooled solution of AlH_3 under stirring condition. After stirring for about 2 hours, excess of the reagent was decomposed by adding moist ether and then water. After drying the ether extract over anhydrous sodium sulphate and filtration, ether was removed by distillation and the residue in the flask was distilled under reduced pressure. The distillate was passed over alumina (neutral, grade II, 1:20). Petroleum ether eluted fraction was rejected and

subsequent fractions eluted with pet.ether-ether (90:10) were collected, solvent removed and the residue distilled under vacuum. The distillate (0.5 g) was found to give a single peak in VPC and a characteristic infrared spectrum of an allylic alcohol.

(b) Reduction of the aldehyde with sodium borohydride

To a solution of sodium borohydride (0.1 g) in isopropyl alcohol (5 ml), a solution of the aldehyde (0.45 g) in isopropyl alcohol (5 ml) was added, the temperature being maintained below 10° during the addition. The mixture was then left overnight at room temperature. A small quantity of water was added and the sodium borohydride complex was decomposed by adding cold dil. hydrochloric acid till the mixture was acidic to congo red. The mixture was then extracted with ether, and the ether extract was successively washed with water, sodium carbonate solution and finally with water. After drying the ether extract over anhydrous sodium sulphate, and filtration, ether was removed by distillation on a water bath. The residue was passed over alumina (neutral, grade II, 1:20) and the first portion eluted with pet. ether was rejected. The subsequent fraction eluted with pet.ether-ether (50:50) was collected, solvent removed, and the residue distilled under vacuum on an oil bath.

The distillate (0.35 g) gave a single peak on VPC and showed the presence of allylic alcohol in infrared spectrum.

The alcohols obtained by reduction with NaBH_4 and AlH_3 were identical. They gave identical infrared spectra and superimposable single peaks in VPC.

b.p. $93-94^\circ/5$ mm., n_D^{26} 1.4512; $(\alpha)_D^{38} + 9.80^\circ$
(c, 5.2; ethanol).

Analysis

Found: C, 77.02; H, 12.94.

Calc. for $\text{C}_{10}\text{H}_{20}\text{O}$: C, 76.86; H, 12.90%.

Infrared spectrum (IR-3)

3400 cm^{-1} (hydroxyl); $1670, 847\text{ cm}^{-1}$ (trisubstituted)

α -Santalene (IV)

This hydrocarbon previously separated from its isomer β -santalene by fractionation and repeated chromatography was further purified by chromatography.

The hydrocarbon (30 g) was passed over alumina (neutral, grade I, 1:20) and eluted with pet.ether. From the eluent, pet.ether was removed by distillation on water bath and the residue was distilled under vacuum on an oil bath. On VPC analysis, the distillate showed two peaks, a major peak resolving earlier accounted for 80%

of the product and was due to α -santalene. The second minor peak accounted for the remaining 20% of the product and was found to coincide with the peak of β -santalene. Further purification of this product by chromatography was not possible. The product gave the following constants:

b.p. 112^o/6 mm., n_D^{27} 1.4757; $(\alpha_D^{27} + 6.37^o)$ (clean).

Analysis

Found: C, 87.78; H, 12.08.

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

Infrared spectrum (IR-5)

3050, 1039 cm^{-1} (cyclopropane system), 1660, 825 cm^{-1} (trisubstituted double bond).

α -Santalol and α -santalal (V and VI)

To a solution of α -santalene (2.04 g) in alcohol (10 ml) in a round bottom flask (50 ml), a solution of selenium dioxide (1.2 g) in alcohol (20 ml) was added. After refluxing the mixture on a water bath for 4 hours, it was filtered through cotton into a separating funnel. The filtrate was diluted with two times its own volume of water and the mixture was repeatedly extracted with ether. The ether extract was washed with water, dried over anhydrous sodium sulphate and filtered. Ether was removed by distillation on a water bath and the

residue was distilled under vacuum on an oil bath. The distillate (0.85 g) was a yellow liquid whose infrared spectrum (IR-6) showed the presence of aldehyde and an alcohol.

Infrared spectra (IR-6)

3050, 1039 cm^{-1} (cyclopropane system);
3400 cm^{-1} (hydroxyl function); 2740, 1690 cm^{-1} (conjugated aldehyde).

Semicarbazone of α -santalal

When α -santalene (10 g) was oxidised according to the method described above, it yielded a mixture (4.5 g) of the aldehyde and alcohol. A solution of the oxidation product (4.5 g) in alcohol (5 ml) was added to a solution of semicarbazide hydrochloride (5 g) and sodium acetate (3 g) dissolved in the least amount of water. The mixture on working up gave the semicarbazone (2.5 g) which was crystallised thrice from alcohol.

m.p. 215-216°

Analysis

Found: N, 15.76.

Calc. for $\text{C}_{16}\text{H}_{25}\text{ON}_3$: N, 15.46%.

Ultraviolet spectrum

λ_{max} . 262 $\text{m}\mu$, ϵ max. 35570.

α -Santalol (V)(a) Reduction with NaBH₄:

The oxidation product (1 g) obtained by the action of selenium dioxide on α -santalene was dissolved in methanol (10 ml) and was treated with a solution of NaBH₄ (0.2 g) in methanol (10 ml). After working up the reaction product as described previously, it showed complete absence of aldehyde function in its infrared spectrum. It was passed through alumina (neutral, gr. II, 1:20). First fraction eluted with pet. ether was rejected. The next fraction eluted with pet. ether-ether (50:50) was collected and solvent removed by distillation on a water bath. The residue was distilled under vacuum on an oil bath and the distillate (0.8 g) showed the infrared spectrum of α -santalol.

(b) Reduction with aluminium isopropoxide

Freshly distilled aluminium isopropoxide (2.8 g) in dry isopropanol (20 ml) was taken in a round bottom flask (100 ml) fitted with a reflux condenser (calcium chloride tube). A solution of the oxidation product (2 g) in dry isopropanol (20 ml) was added to the flask and the mixture was refluxed on an isomantle for 8 hours. During the reduction with aluminium isopropoxide,

acetone is always liberated and unless it is removed, the reaction does not go to completion. By occasionally stopping the water supply in the condenser, acetone was allowed to escape. After heating for 8 hours, the vapours were allowed to pass through a test tube containing 2,4-dinitrophenyl hydrazine solution which gives a precipitate for a ketone.

After refluxing for 8 hours, the escaping vapours failed to give any test for acetone with the DNP reagent and the reaction was complete. The refluxing was continued for another 2 hours, after which the mixture was cooled, ice water was added and the Al-complex formed was decomposed by adding cold dil.HCl till the mixture was acidic to congo red. The mixture was thrice extracted with ether and the ether extract successively washed with water, Na_2CO_3 solution and finally with water. After drying the ether-extract over anhydrous sodium sulphate and filtration, ether was removed by distillation. The residue showed complete absence of aldehyde function in its infrared spectrum and was passed over alumina (neutral, grade II, 1:20) and eluted with pet.ether. The pet.ether fraction was discarded and the fractions eluted with pet.ether-ether (50:50) were collected. After removing the solvent, the residue was distilled under vacuum on an oil bath.

The distillate (1.5 g), a colourless liquid, was α -santalol.

α -Santalols obtained by reduction with iso-^{Al-}propoxide and with NaBH₄ showed identical infrared spectra and other properties.

b.p. 123-124°/1 mm., n_D^{26} 1.5031; $(\alpha)_D^{32} + 16.94^\circ$ (c, 5.37). High rotations of α -santalol obtained is noteworthy.

Analysis

Found: C, 81.40; H, 11.19.

Calc. for C₁₅H₂₄O: C, 81.76; H, 10.98%.

Infrared spectrum (IR-7).

3050, 1035 cm⁻¹ (cyclopropane system), 3400 cm⁻¹ (hydroxyl function); 1665, 825 cm⁻¹ (trisubstitution).

β -Santalene (VII)

A sample of β -santalene (30 g) obtained from the laboratory stock was passed over alumina (neutral, gr. I, 1:20) and eluted with pet. ether (40-60°). From the eluent, pet. ether was removed by distillation, and the residue was refluxed and distilled over sodium. The distillate showed two peaks (VPC). One major, resolving earlier, was β -santalene accounting for 66% of the product injected and the other was a hydrocarbon possibly epi- β -santalene, accounting for the remaining 33%. The distillate gave the following constants:

b.p.124°/7 mm., n_D^{27} 1.4913; $(\alpha)_D^{27}$ - 72.86° (clean).

Analysis

Found: C, 87.72; H, 11.37.

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

Infrared spectrum (IR-8)

1650, 880 cm^{-1} (exomethylene double bond),
817 cm^{-1} (trisubstitution).

β -Santalol and β -santalol (VIII and IX)

Purified β -santalene (2 g) was dissolved in alcohol (10 ml) in a round bottom flask and after adding a solution of SeO_2 (1.6 g) in alcohol (20 ml), the mixture was refluxed on water bath for 4 hours. The reaction product was worked up in the usual manner. The final product (1.3 g) was a mixture of the aldehyde and alcohol as shown by infrared spectrum.

Infrared spectrum (IR-9)

3450 cm^{-1} (hydroxyl function); 2710, 1690 cm^{-1} (conjugated aldehyde).

The reaction was repeated several times and the oxidation product was used for various reactions.

Semicarbazone of β -santalol

To a mixture of semicarbazide hydrochloride (6 g) and sodium acetate (9 g) in the least amount of water,

the oxidation product (5 g) was added and after working up as usual, crude semicarbazone was obtained. This was crystallised two times from alcohol when pure semicarbazone (2.9 g) of β -santalal was obtained.

m.p. 207°

Analysis

Found: N, 15.65.

Calc. for $C_{16}H_{25}ON_3$: N, 15.46%.

Ultraviolet spectrum

λ_{max} . 263 m μ , ϵ max. 37010.

β -Santalol (VIII)

(a) Reduction with $NaBH_4$

The oxidation product (1 g) in methanol (5 ml) was treated with a sodium borohydride (0.211 g) in methanol (10 ml). After working up the reaction mixture as usual, β -santalol (0.85 g) was obtained as the reduction product.

(b) Reduction with aluminium isopropoxide

Freshly distilled aluminium isopropoxide (3 g) in dry isopropanol (15 ml) and the oxidation product (2 g) in dry isopropanol (20 ml) were refluxed together under dry conditions. After carrying out the reaction and

working up the product in the same way as in the case of α -santalene, β -santalol was obtained.

The alcohols obtained by reduction with NaBH_4 and with aluminium isopropoxide gave identical infrared spectra and superimposable single peaks on VPC.

The alcohol gave the following constants:

b.p. $130-32^\circ/1$ mm., n_D^{25} 1.5111; $(\alpha)_D^{25} - 53.47^\circ$ (c, 5.05).

Analysis

Found: C, 81.83; H, 10.8.

Calc. for $\text{C}_{15}\text{H}_{24}$: C, 81.76; H, 10.98%.

Infrared spectrum (IR-10)

3450 cm^{-1} (hydroxyl function); 1655, 878 cm^{-1} (exomethylene double bond), 817 cm^{-1} (trisubstitution).

Tetrahydro- β -elemene (X)

Elemol (Xa) obtained from the tail fractions of Java citronella oil was used for the preparation of the hydrocarbon.

The tail fraction (375 g) of Java citronella oil was totally distilled under vacuum (1-2 mm). The distillate (350 g), boiling upto $123^\circ/1-2$ mm was collected and subjected to fractionation on Todd's column. Various fractions collected are shown in Table 1.

TABLE 1

No.	Vacuum	Temp. range	Quantity
1	1 mm.	69-102°	217 g.
2	1 mm	102-107°	125 g.
3	Residue		8 g.

From fraction 2 above, a portion (65 g) was chromatographed over alumina (2 kg; neutral, gr.II) and the following fractions were collected (table 2).

TABLE 2

No.	Eluent	Volume (lit)	Quantity (g)	Remarks
1	Pet.ether (40-60°)	3.0	6.0	yellowish viscous liquid, does not solidify.
2	Pet.ether (90%) + Benzene (10%)	4.0	8.0	thick viscous liquid, does not solidify.
3	Pet.ether (50%) + Benzene (50%)	6.0	40.0	thick viscous liquid, solidifies in the cold.
4	Benzene	3.0	4.0	yellowish, non-solidifying liquid.

Fraction 3 (table 2) gave a solid (40 g) which was almost pure elemol. For further purification, it was rechromatographed over alumina with greater ratio (2 kg, neutral gr.II). Various fractions collected are shown in Table 3.

TABLE 3

No.	Eluent	Volume (lit)	Quantity (g)	Remarks
1	Pet.ether (40-60°)	3.0	nil	-
2	Pet.ether (80%) + Benzene (20%)	4.0	2.5	slightly yellowish liquid, does not solidify.
3	Pet.ether (50%) + Benzene (50%)	5.0	37.0	thick viscous liquid solidifies quickly in cold.
4	Benzene	3.0	traces	non-solidifying.

Fraction 3 (table 3) gave pure elemol (37 g) which showed the following constants:

m.p. 51°; $(\alpha)_D^{28} - 5.8^\circ$ (c, 3.4); VPC single peak.

Infrared spectrum

3450 cm^{-1} (hydroxyl function); 1650, 915 cm^{-1} (vinyl), 1650, 892 cm^{-1} (methylene).

Tetrahydro elemol (Xb)

Elemol (12.2 g) was dissolved in pure glacial acetic acid (150 ml) in a hydrogenation flask (1 lit). Hydrogenation was carried out in presence of freshly prepared Adams' platinum oxide catalyst (0.4 g). A

volume of hydrogen corresponding to 2.4 litres of hydrogen at N.T.P. was absorbed, indicating that both the double bonds were fully hydrogenated. The mixture was then filtered and poured into large excess of water, repeatedly extracted with ether. The ether extract was washed with water, sodium carbonate solution and finally with water and then dried over anhydrous sodium sulphate. After filtration, ether was removed by distillation, when a thick residue (11.8 g) of tetrahydro elemol was obtained.

The disappearance of bands at 892 and 1650 cm^{-1} in the infrared spectrum of the thick residue clearly indicated that both the double bonds in elemol were completely hydrogenated.

Tetrahydroelemol benzoate (Xc)

Tetrahydroelemol (11 g) was dissolved in dry pyridine (50 ml) in a round bottom flask (100 ml). Freshly distilled benzoyl chloride (20 ml) was added to it and after keeping for 24 hours in anhydrous condition, it was refluxed on an isomantle for about 2 hours. The mixture was then poured over crushed ice and extracted with ether. From the ether extract, pyridine was removed by repeated washing with water, and then cold dil. hydrochloric acid. The ether extract was then made free from hydrochloric acid by successively washing with water,

sodium carbonate solution, and finally with water. The ether extract was dried over anhydrous sodium sulphate, filtered and ether removed by distillation, when a residue (25 g) of tetrahydroelemol benzoate, benzoic acid and benzoic anhydride was obtained.

Tetrahydro- β -elemene (X)

The crude benzoylated product (25 g) was taken in a distillation flask (100 ml) and pyrolysed under a vacuum of 100 mm at 210-230°. Benzoic acid, benzoic anhydride and tetrahydro- β -elemene passed over and collected in the receiver.

The pyrolysed material extracted with ether and the ether extract was thoroughly washed with caustic soda solution, then with water and dried over anhydrous sodium sulphate. After filtration and distilling off ether, the residue was passed over alumina (neutral, grade I, 1:60) and eluted with pet.ether. Pet.ether was removed by distillation and the residue was distilled on an oil bath under vacuum. The distillate, tetrahydro- β -elemene (9 g) was further purified by refluxing and distillation over sodium.

b.p. 119°/10 mm., n_D^{28} 1.4705; $(\alpha)_D^{28}$ - 7.6° (clean),
VPC single peak.

Analysis

Found: C, 86.57; H, 13.61.
Calc. for C₁₅H₂₈: C, 86.46; H, 13.54%.

Infrared spectrum (IR-11)

3100, 1775, 1643, 888 cm^{-1} .

Tetrahydro- β -elemenol and tetrahydro- β -elemenal(XI & XII)

Tetrahydro- β -elemene (2 g) was dissolved in alcohol (10 ml) and refluxed with a solution of selenium dioxide (1.7 g) in alcohol (20 ml) in a round bottom flask (50 ml). After refluxing for 6 hours, the reaction mixture was filtered through cotton and collected directly into a separating funnel. It was diluted with double its volume of water and repeatedly extracted with ether. The ether layer was washed with water, dried over anhydrous sodium sulphate, filtered, and ether removed by distillation on a water bath. The residue was distilled under vacuum on an oil bath. The distillate (0.7 g) showed presence of both aldehyde and alcohol in infrared spectrum.

Infrared spectrum (IR-12)

3440 cm^{-1} (hydroxyl function); 2740, 1695 cm^{-1} (conjugated aldehyde), 1631, 900 cm^{-1} (disubstitution).

Semicarbazone of tetrahydro- β -elemenol

Semicarbazide hydrochloride (0.3 g) and sodium acetate (0.5 g) were dissolved in the least amount of

water. The oxidation product (0.2 g) was added to this solution. After adding alcohol (3 ml), the solution was warmed on a water bath and kept aside overnight when crude crystals of the semicarbazone deposited. The crude product was filtered, washed with water and recrystallised from hot alcohol, when pure crystalline semicarbazone (0.085 g) was obtained, m.p. 208-209°.

Analysis

Found: N, 15.24.

Calc. for $C_{16}H_{29}ON_3$: N, 15.16%.

Ultraviolet spectrum

λ_{max} . 260.5 μ ; ϵ max. 21350.

Tetrahydro- β -elemenol (XI)

A mixture of the oxidation product (2 g) in dry isopropanol (10 ml) and freshly distilled aluminium isopropoxide (2.5 g) in dry isopropanol (20 ml) was refluxed under dry conditions. The refluxing was continued till the acetone formed in the reaction was completely removed. The reaction product was worked up as previously and chromatographed over alumina (neutral, gr. II, 1:30). First portion eluted with pet. ether was set aside. Subsequent fraction eluted with pet. ether-ether (50:50) was distilled to remove the solvent and

the residue was distilled under vacuum on an oil bath when a colourless distillate (0.5 g) was obtained.

b.p.133-35°/1 mm., n_D^{30} 1.4952; $(\alpha)_D^{30} + 57.06^\circ$ (c,4.75).

Analysis

Found: C, 79.89; H, 12.54.

Calc. for $C_{15}H_{28}O$: C, 80.29; H, 12.53%.

Infrared spectrum (IR-13):

3420 cm^{-1} (hydroxyl fraction), 1640, 895 cm^{-1}
(methylene double bond).

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