terpenoids

synthesis of terpenoid lactones and
transformations of (+) ar-turmerone and (−) carvone
thesis submitted to
the university of poona
for the degree of
doctor of philosophy
in chemistry
by

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essential oils division
national chemical laboratory
poona
india

C O N T E N T S

GENERAL REMARKS

1. The melting points and boiling points are uncorrected.

2. All temperatures are recorded on the Centigrade scale.

3. The ultraviolet spectra were recorded on Beckman DK-II ratio recording spectrophotometer.

4. The infrared spectra were recorded on a Perkin-Elmer infracord spectrophotometer, Model 137B and Model 221 with sodium chloride optics.

5. The N.M.R. spectra were measured in carbon-tetrachloride solution unless otherwise mentioned using tetramethylsilane as internal reference on A-60 Varian instrument and the chemical shifts were measured in τ units.

6. The acid washed activated alumina standardised as per Brockmann's procedure was employed for column chromatography.

7. Gas liquid chromatographic analysis were carried out on a Griffin & George GLC apparatus MK II^{A} employing hydrogen as carrier gas.

8. The list of references pertaining to each part has been given at the end of that part.

9. The numbers given to the charts and numbers given to the figures in each chapter of the thesis refer to that particular part only.

10. All the I.R. spectra and N.M.R. spectra are given in the end of the thesis.

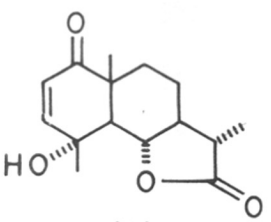
11. Silica gel (200 mesh; prepared in the Fine Chemical Project, National Chemical Laboratory) with 15% of plaster of Paris (200 mesh; commercial quality) as binder, was used for T.L.C.

+++

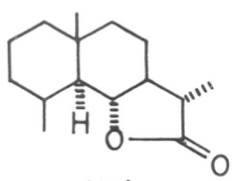
chapter 1

synthesis of terpenoid lactones

A large number of 1-oxygenated eudesmanes occur in nature (Chart 1). An interesting compound belonging to this group is tauremisin (vulgarin) which was isolated from the flower of *Artemisia taurica* Willd by Rybalko and Dolejs[7] and from *Artemisia vulgaris* L. by Geissman and Ellestad.[8] The structure (I) has been assigned to tauremisin on the basis of spectral data and degradation work shown in Chart II.[7] Its conversion to santanolide C (II) establishes the carbon skeleton, the mode of attachment of the lactone ring and the stereochemistry at C_5, C_6, C_7, C_{10} and C_{11}. Its transformation to the β,γ-unsaturated ketone (III) with Zn - acetic acid and its preparation from the base catalysed elimination of the keto-diol (IV) establish the positions of the keto-group, -OH group and the double bond.



(I)



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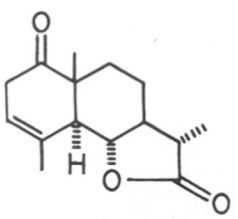

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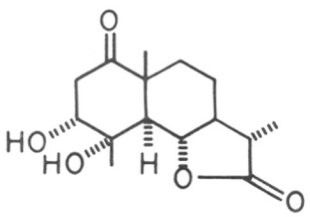

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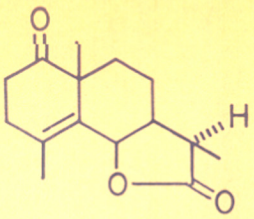

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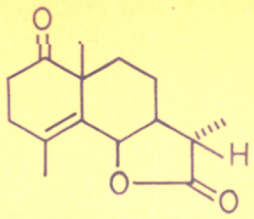
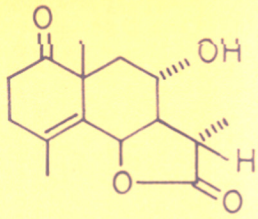
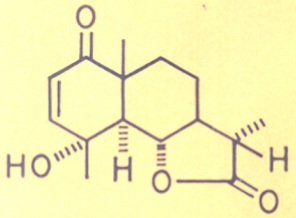


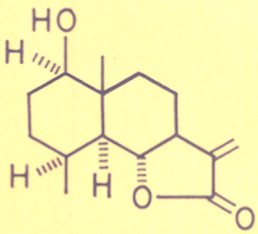
DESOXY-Ψ-SANTONIN(2,3,4)



Ψ-SANTONIN (3,4,5,6)



TAUREMISIN(2,3,7,8)



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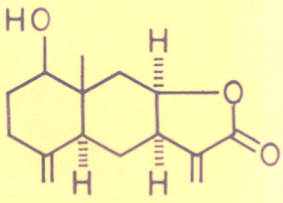

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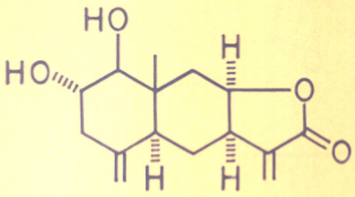

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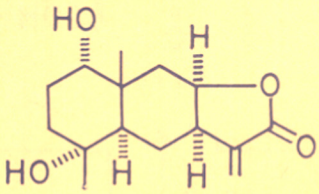

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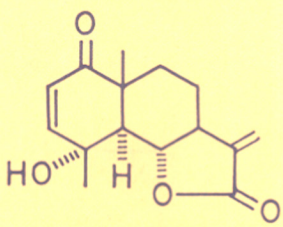

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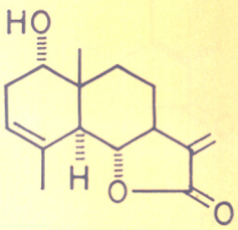

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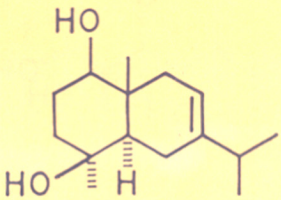

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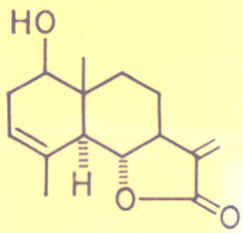

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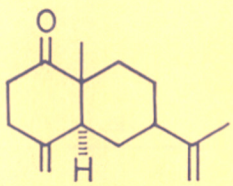

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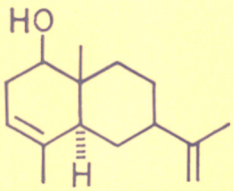


DICTYOPTEROL (16)

CHART I

1-OXYGENATED EUDESMANES

(THE NUMBERS IN THE BRACKETS REFER TO THE NUMBERS OF THE REFERENCES)

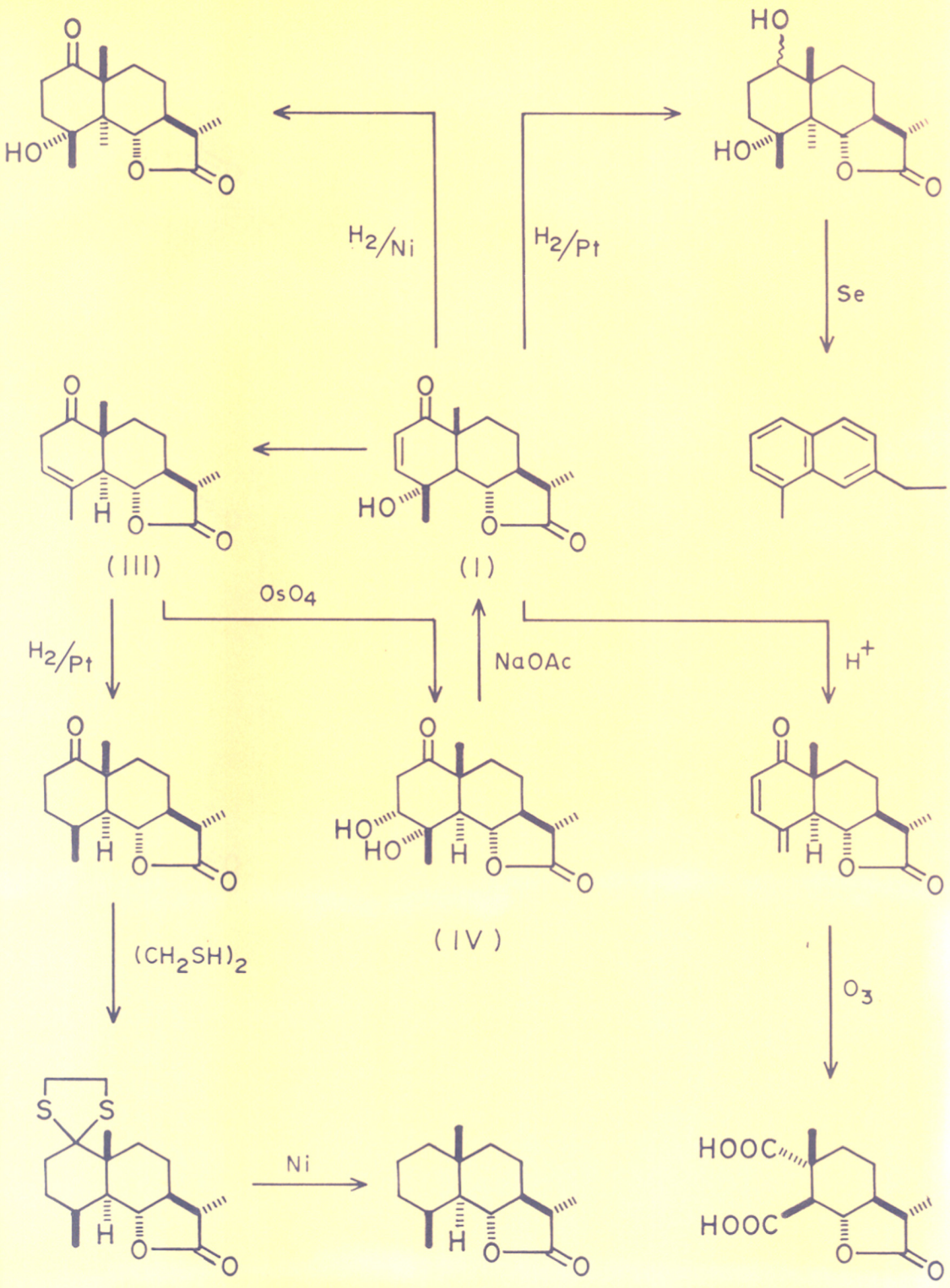
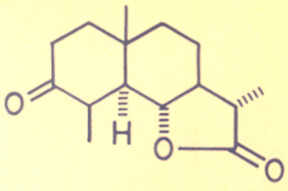


CHART II

TAUREMISIN AND RELATED COMPOUNDS



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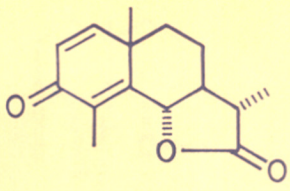

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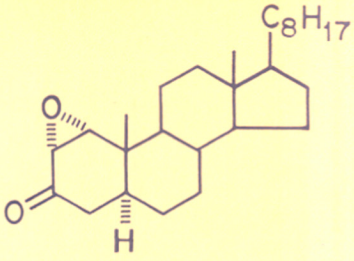

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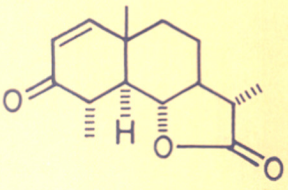

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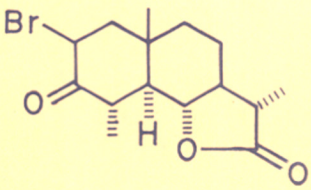

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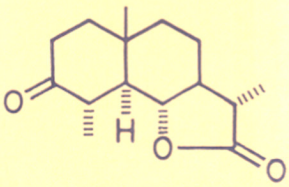

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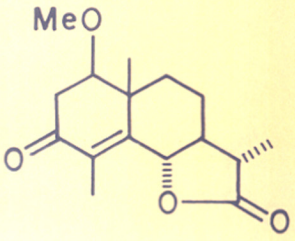

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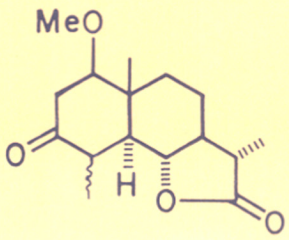

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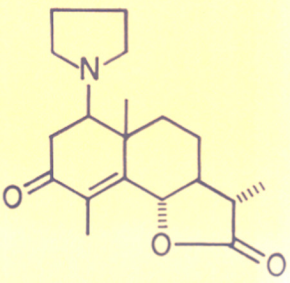

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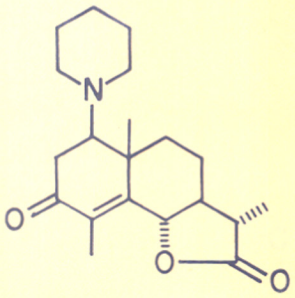

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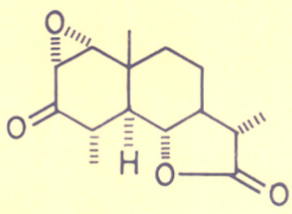

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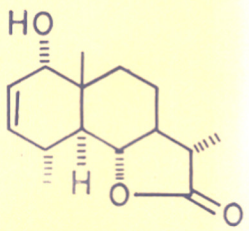

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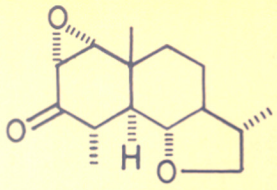

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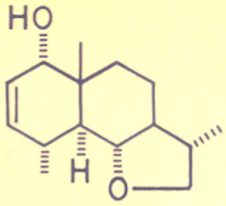

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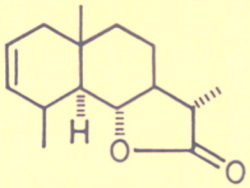

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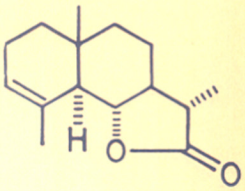

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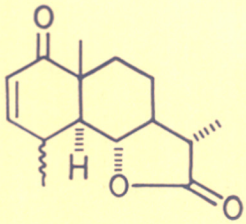

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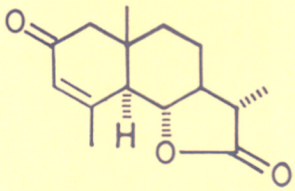

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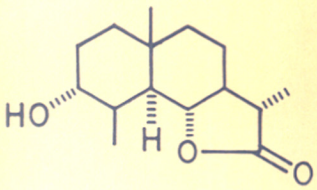

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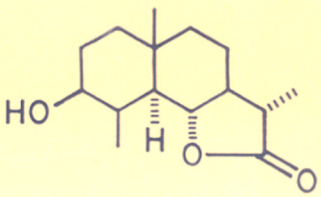

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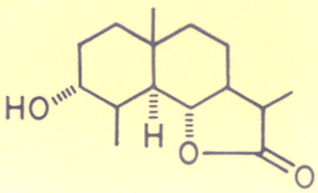

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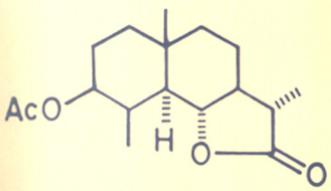

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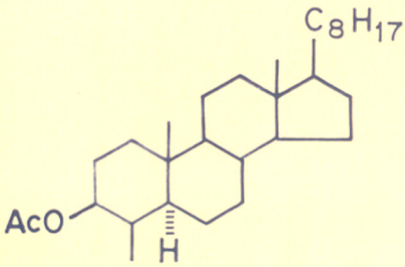

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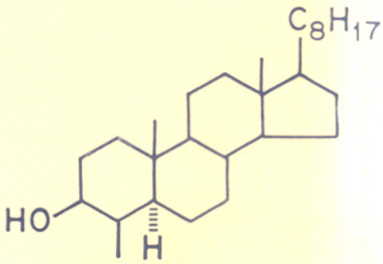

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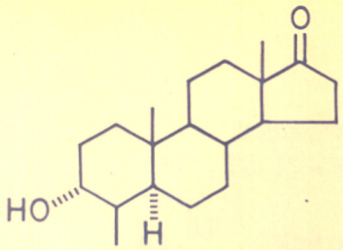

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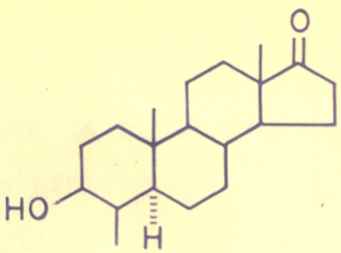

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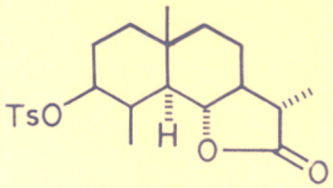

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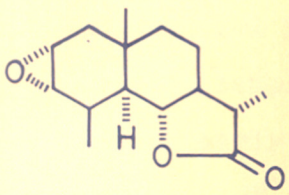

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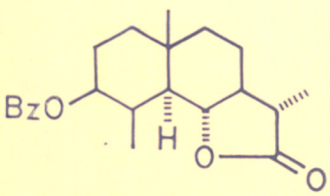

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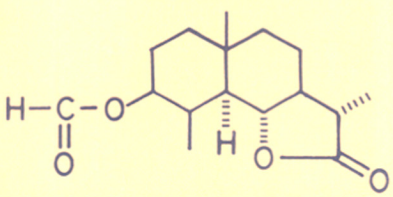

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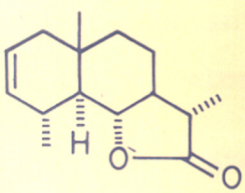

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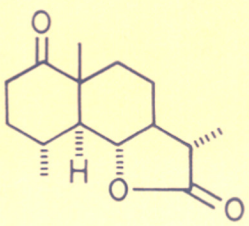

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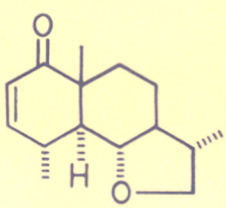

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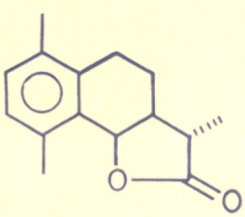
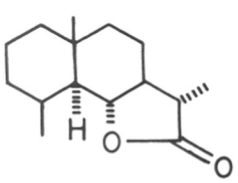


(XXXVIII)

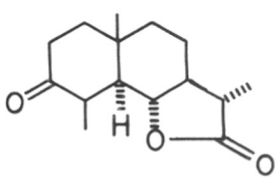
Santanolide C (4,5,11α(H)-6β(H)-eudesman-6,13-olide) (II)[7,8,15,17-20] was first prepared from santonin by Kovacs et al.[17] Hydrogenation of santonin (room temperature, 120 atm. pressure) furnished the hydroxylactone m.p. 135°, $(\alpha)_D$ + 42 ± 1°, which was oxidised to 3-oxo-santanolide C (V). The ethylenedithioderivative of (V) on desulphurisation with Raney nickel furnished santanolide C. The constants reported for this sample of santanolide C (m.p. 136-137°C; $(\alpha)_D$ + 92.8 ± 3°) clearly show that it is not pure; pure santanolide C[7] has m.p. 155°, $(\alpha)_D$ + 54.8°. Santanolide C has proved useful in elucidating the structure of some naturally occurring lactones; it has also been employed for the synthesis of dihydrojunenol.[20] The methods of preparation of santanolide C from santonin[17,21] and dihydroeudesmol[22] unambiguously establish its stereochemistry.

Santonin (VI) has been employed by us as the starting material for the synthesis of tauremisin since:

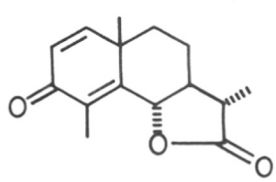
1. It is readily available.
2. Its stereochemistry has been rigorously established both by chemical[23] and X-ray methods.[3,24]
3. It is closely related to tauremisin.
4. It is a highly crystalline compound and its purity can be easily checked.



(II)



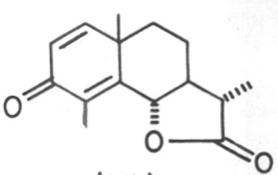
(V)



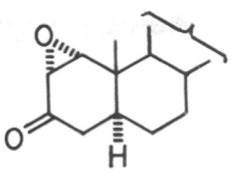
(VI)

The conversion of santonin to a suitable intermediate for the synthesis of tauremisin involves: (i) removal of oxygen function from C_3, (ii) intrdduction of oxygen at C_1, and (iii) introduction of a double bond at C_2 - C_3 or C_3 - C_4. Survey of steroid literature[25] shows that comparable transformations have been effected in the conversion of the α,β-epoxyketone (VII) to Δ^2-cholesten-1α-ol through reduction with hydrazine. This elegant approach to the synthesis of 1-oxosteroids is superior to the earlier methods and hence we became interested in studying the hydrazine reduction of the α,β-epoxyketone (XV) with a view to prepare the allylic alcohol (XVI).

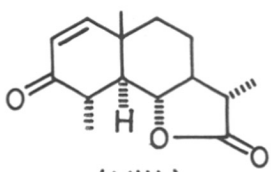
The α,β-unsaturated ketone (VIII) has been prepared in rather low or moderate yields by Yanagita and Tahara[26] and Hendrickson and Bogard[27] through the dehydrobromination of the bromocompound (IX). In our hands the dehydrobromination



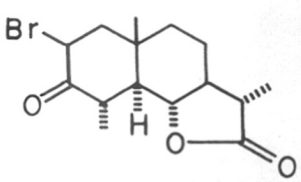
(VI)



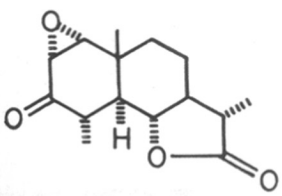
(VII)



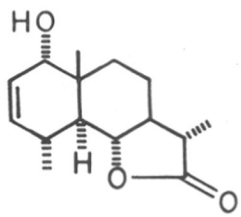
(VIII)



(IX)



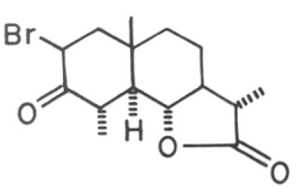
(XV)



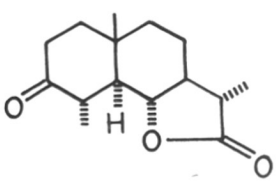
(XVI)

of (IX) employing Hendrickson's conditions proceeded in rather low yield. The dehydrobromination product shows a carbonyl band in its I.R. spectrum at 1715 cm^{-1} suggesting the probable presence of α-tetrahydrosantonin (X). Probably (X) is formed from the bromo compound (IX) on refluxing with collidine; there are analogies in literature for similar types of reduction.[28]

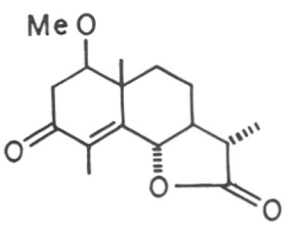
Since the yield in the dehydrobromination step was rather poor we explored a different approach. The Michael addition of alcohols such as methanol to conjugate ketones proceeds smoothly.[29,30] It was hoped that controlled addition of methanol to santonin in the presence of a base would furnish the 1-methoxylactone (XI). We considered that the alternate mode of addition involving attack of $^{\ominus}OMe$ on C_5 may be somewhat difficult since the OMe will have to occupy an angular position. The 1-methoxylactone (XI)



(IX)

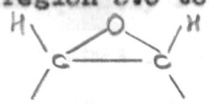


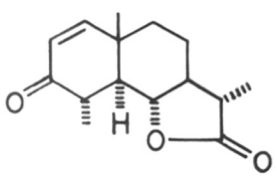
(X)



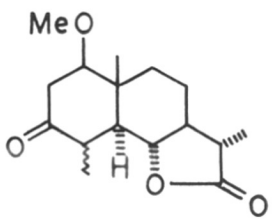
(XI)

was expected to yield on hydrogenation the dihydrocompound (XII) which on treatment with base can furnish (VIII). However, attempted addition of methanol to santonin furnished only the unreacted starting material. The attempted addition of pyrrolidine and piperidine to santonin[31] to furnish (XIII) and (XIV) did not prove fruitful. Hence the α,β-unsaturated ketone (VIII) was prepared by the method of Hendrickson.

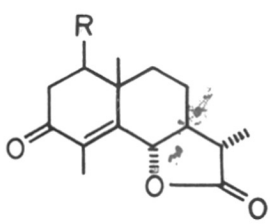
The ketone (VIII) on treatment with H_2O_2 in the presence of alkali[33] furnished the epoxide (XV). The product has the expected structure as shown by elemental analysis, I.R. spectrum (ν_{max} at 1720 cm^{-1}; whereas starting material showed the band due to conjugated ketone at 1687 cm^{-1}), U.V. spectrum (no strong absorption at 227 mμ showing that the conjugated double bond originally present in (VIII) has reacted) and NMR spectrum (no signals in the vinyl proton region 3.0 to 4.5τ; but two proton signals at 6.77τ due to ). The stereochemistry at C_1 and C_2

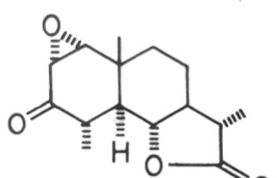


(VIII)

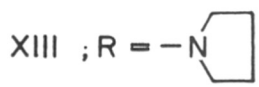


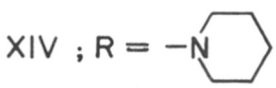
(XII)





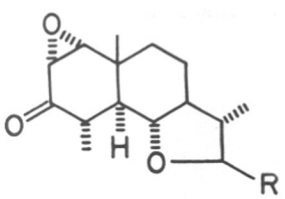
(XV)

XIII ; R = 

XIV ; R = 

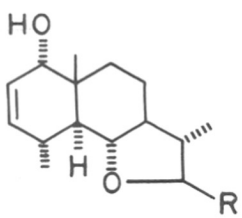
has been assigned on the basis of analogy with epoxide formed from similarly constituted cholest-1-en-3-one, and is in agreement with its optical rotatory dispersion curve which shows a positive Cotton effect with amplitude of a = + 64. This is comparable with the ORD curve of 1,2α-oxido-cholestan-3-one (a = + 93).[32]

The hydrazine reduction of the oxido compound (XV)[25,34] furnished in poor yield a product which showed a band at 3390 cm^{-1} in its I.R. spectrum probably due to the presence of the allylic alcohol (XVI). However, no crystalline material could be isolated from the reaction mixture and the hydrazine reduction of (XV) was not further studied. It was considered that the low yield of the required product may be due to reaction of lactone group with hydrazine and satisfactory results may be obtained by carrying out the hydrazine reduction of the ketone (XVII). Dr. Honwad and Dr. Rao[35] have subsequently studied the hydrazine reduction of (XVII) which furnishes in satisfactory yields the allylic alcohol (XVIII). The allylic alcohol was then transformed to tauremisin.



XV ; R = O

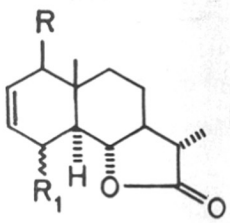
XVII ; R = H_2



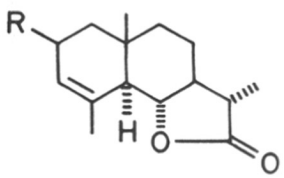
XVI ; R = O

XVIII ; R = H_2

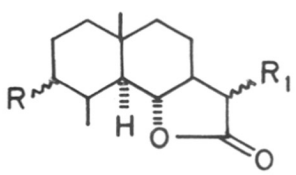
Since the hydrazine reduction of (XV) did not proceed in the expected fashion we wanted to study the allylic oxidation of the unsaturated lactones (XIX) and (XX). (XIX) on allylic oxidation was expected to furnish the 1-oxo- compound (XXI), a potential intermediate for the synthesis of tauremisin. (XX) on allylic oxidation was expected to furnish the 2-oxo compound (XXII), which we hoped to transform after a number of steps to the 1-oxo compound (XXI). The unsaturated lactones (XIX) and (XX) have been previously prepared in poor yields by Cocker and McMurry[36] by dehydrating the hydroxylactone (XXIV),* m.p. 108-110°, $(\alpha)_D$ = + 36.0° with $POCl_3$ and pyridine.



XIX ; R = H_2 ; R_1 = β-Me
XXI ; R = O ; R_1 = Me



XX ; R = H_2
XXII ; R = O



XXIV ; R = β-OH; R_1 = α-Me
XXV ; R = α-OH ; R_1 = β-Me

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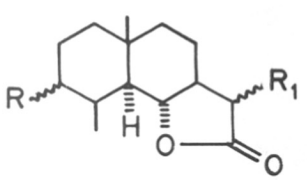
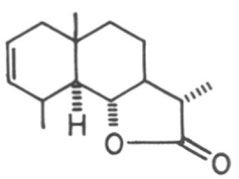
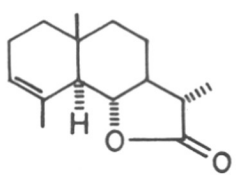
* It may be noted that the stereochemistry at C_3 and C_{11} shown here is different from that proposed by Cocker and McMurry (XXV). Recent X-ray work[3,24] has shown that in (-) α-santonin, C_{11}-Me is α and hence the configurations at C_{11} of all compounds in ref. 36 has to be changed. The arguments for revising the configuration at C_3 are discussed in the sequel.

A systematic study of the elimination reactions of (XXIV) and its esters was then undertaken to find out optimum conditions for the preparation of the unsaturated lactones (XIX) and (XX).

One of the hydrogenation products of santonin is a hydroxy lactone, m.p. 108-110°, $(\alpha)_D$ + 36° for which structure (XXV) has been assigned by Cocker and McMurry.[36] The arguments in favour of the α-configuration for C-3 hydroxyl are not compelling and available data are best explained by structure (XXIV). Sodium borohydride reduction of keto-lactone (V) furnishes exclusively the hydroxy lactone m.p. 108-110°.[21] Arguing strictly from the steric view point, hydride attack on the C-3 carbonyl of (V) from the β-face, which would be necessary for 3-α-ol formation is prevented by steric interference of C-4 β-methyl group.[37] The hydroxy lactone is also formed stereospecifically during the catalytic hydrogenation of (V);[21] due to the shielding of the β-side by the methyl groups at C_4 and C_{10}, the attack is likely to take place from the α-side to furnish 3β-ol. It is







V ; R = O ; R_1 = α-Me

XXIV; R = β-OH ; R_1 = α-Me XIX XX

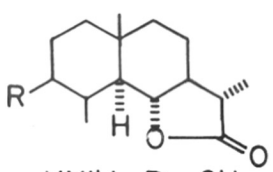
XXV ; R = α-OH ; R_1 = β-Me

interesting to note that hydrogenation of 1-oxo and 12-oxo steroids[38], which have an axial methyl group at an adjacent carbon atom gives exclusively equatorial alcohols; these results show that Barton's generalisation* is an oversimplification.

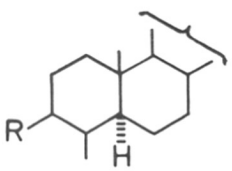
The molecular rotation increament (ΔM_D = -46) for acetylation of the hydroxy lactone is of the same sign and magnitude as molecular rotation increament (ΔM_D = - 95) for acetylation of 4β-methylcholestanol (XXVIII).[40] It is to be noted that the steroidal compounds chosen as reference materials for M_D are ideally suited for comparison with (XXIV) and (XXVI) since both sets of compounds have:

1. trans fused decalin ring system, and
2. axial methyl groups at C_4 and C_{10}.

In view of similarity in stereochemistry at C_4, C_5 and C_{10} the conformations of A-B ring system of (XXVI) and (XXVII) are likely to be identical; (XXIV) and (XXVIII) are also expected to have identical conformations of A-B ring system.



XXIV ; R = OH
XXVI ; R = OAc

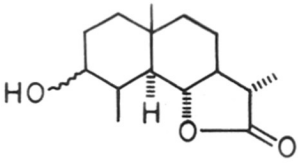


XXVII ; R = OAc
XXVIII ; R = OH

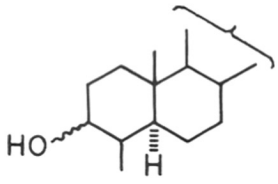
* Catalytic hydrogenation of both hindered and unhindered ketones in strongly acid media (rapid hydrogenation) affords the axial alcohol.[39]

Recently Eliel[41] has developed a convenient approach to calculate the chemical shifts due to carbinol protons in the N.M.R. spectra of substituted cyclohexanols. This approach employs a set of empirical parameters, distinct for each alkyl group in each position with respect to each type of carbinol hydrogen. From values cited in literature for the chemical shifts of carbinol protons of androsterone and epiandrosterone[42] and the parameters given by Eliel, we have calculated the chemical shifts (for carbinol proton) of 4β-methylandrosterone (XXIX) ($-\nu$ =224 c.p.s. (6.27τ) and 4β-methylepiandrosterone (XXX) ($-\nu$ 226.5 c.p.s.) (6.23τ). Hence the hydroxylactones (XXIII) and (XXIV) may be expected to show signals at 6.27τ and 6.23τ due to carbinol protons. It is evident that the chemical shifts of the carbinol protons cannot be used to distinguish the epimeric alcohols (XXIII) and (XXIV).

However, the signal width of the carbinol proton is expected to be different for the epimeric alcohols (XXIII) and (XXIV). The equatorial proton of (XXIII) at C_3 is expected to give a sharp signal; the signal of axial C-3



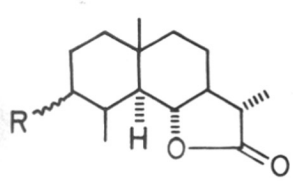
(XXIII): α-OH
(XXIV): β-OH



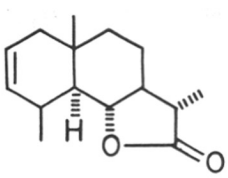
(XXIX): α-OH
(XXX): β-OH

proton of the epimeric alcohol (XXIV) is expected to be broad. The same relationship will also hold good in the case of the corresponding acetates. The N.M.R. spectrum of the acetate (XXVI) prepared from the hydroxy lactone (XXIV) exhibits a broad signal at 5.13τ due to C_3-H and suggests that the C-3 acetate is equatorial.[46]

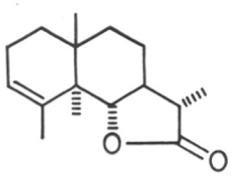
To confirm the C-3 stereochemistry of the hydroxy-lactone (XXIV) it was considered desirable to prepare the epimeric alcohol (XXIII). Attempts to prepare the hydroxy-lactone (XXIII) by heating the tosylate (XXXI) with dimethyl-formamide[43,44] at 70° for 72 hrs resulted mainly in the formation of elimination products. Hydrogenation of epoxide* (XXXII) did not proceed satisfactorily, probably due to the presence of axially oriented methyl groups at C_4 and C_{10}. The hydroboration of the lactone (XXIIa) appeared to be attractive for the preparation of the hydroxylactone (XXIII), but has not been studied by us.+



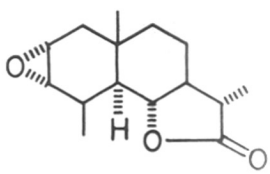
(XXIII): R=α-OH
(XXIV): R=β-OH
(XXVI): R=β-AcO
(XXXI): R=β-TsO



(XIX)



(XX)



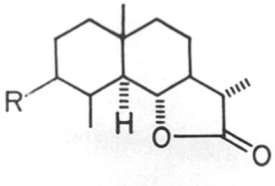
(XXII)

* Prepared by action of perbenzoic acid on (XIX).

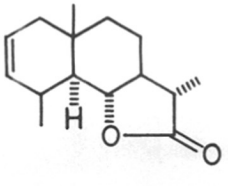
\+ Dr. Kulkarni and Dr. Kadival have kindly informed us that they are investigating the hydroboration of the lactone (XXIIa). Hence we have not utilised this approach.

The tosylate (XXXI) was dissolved in dimethylaniline and heated under reflux for 30 min., however, this did not result in elimination. The benzoate (XXXIII) was recovered unchanged after heating under reflux in dimethylaniline solution. Heating the hydroxylactone (XXIV) under reflux in acetic acid solution in the presence of p-toluene sulphonic acid did not furnish the unsaturated lactone (XIX) or (XX); however, the corresponding acetate (XXVI) was produced in excellent yields.

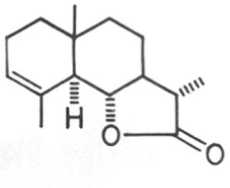
Some alcohols have been dehydrated with tosyl chloride in dimethylformamide-collidine mixture in presence of SO_2.[45] Treatment of the hydroxylactone (XXIV) with the above reagent at 5-20° furnished a solid lactone (ν_{max} 1780 cm^{-1}), m.p.195°, which did not contain sulphur. The elemental analysis indicated that the product had the molecular formula $C_{16}H_{24}O_4$. The I.R. spectrum (ν_{max} 1720 cm^{-1} and 1190 cm^{-1}, no band at 3400 cm^{-1} indicating absence of OH group) of the product and its molecular formula which differed from the starting compound by one carbon atom and one oxygen atom suggested that it may be



(XXIV): R=OH
(XXXI): R=OTs
(XXXIII): R=OBz

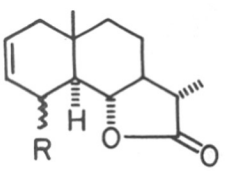


(XIX)

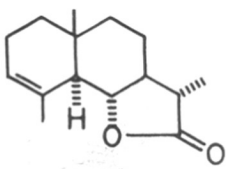


(XX)

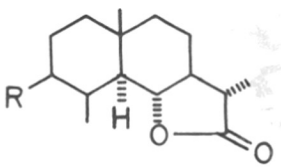
the formate (XXXIV). This was further supported by the conversion of the product, m.p. 195° to the starting hydroxy-lactone (XXIV) by saponification with alkali. Treatment of the tosylate (XXXI)[21] with potassium tertiary butoxide in dimethyl sulphoxide[47] furnished a 5:1 mixture of (XX) and (XIX) (analysis by NMR and IR spectra). The benzoate (XXXIII), m.p. 185-187°, $(\alpha)_D$ = + 68° (c 3; $CHCl_3$) on pyrolysis at 350° furnished in excellent yield Δ^2-santenolide* (XIX).



XIX ; R = β-Me
XXXV ; R = α-Me



XX



XXIV ; R = OH
XXXIII ; R = OBz
XXXV ; R = $-O-\overset{\overset{O}{\|}}{C}-H$

XXXI ; R = OTs

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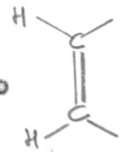
* It may be of interest to note that M_D of (XIX) is higher than that of its C_4 epimer[48] (XXXV) by + 215°. This is in agreement with one of the generalisations of Mills[49,50] who has stated that derivatives of the type (XIX) are more dextrorotatory than those of type (XXXV) and that the difference (M_D = + 200°) is approximately independent of the presence of additional substituents in the cyclohexene ring, provided that they have the same configuration in any pair of β-methyl cyclohexenes which are compared.

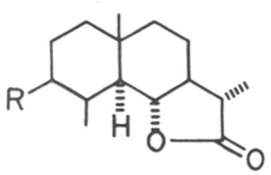
The pyrolysis product was identified as (XIX) on the basis of:



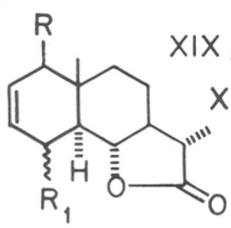
1. its method of preparation
2. I.R. spectrum ($\nu^{CS_2}_{max}$ 720 cm^{-1} due to
3. N.M.R. spectrum (2 proton signal at 4.40 τ ; 3 protons doublet at 8.93 τ due to C_4-Me.
4. its m.p. and rotation which are in reasonable agreement with the previously reported values for (XIX).

Hydrogenation of (XIX) furnished santanolide C (II). The route santonin (XXIV) (XXXIII) (XIX) (II) offers a convenient method* for the preparation of santanolide C from santonin and is superior to the methods described in literature.

Oxidation of (XIX) with sodium dichromate[52,53] in acetic acid at 100° for 6 hours furnished a product having ν_{max} 1775, 1725, 1665 cm^{-1} and λ_{max} = 235 mμ (ε 4390). The spectral data clearly show that the product is not composed exclusively of the keto-lactone (XXI) the anticipated allylic oxidation product. The spectral data suggest that oxidation



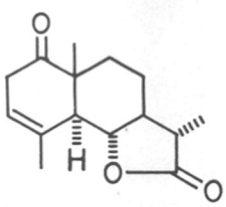
II ; R = H_2
XXIV ; R = OH
XXVI ; R = OAc



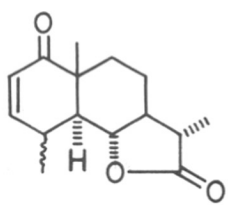
XIX ; R = H_2; R_1 = β-Me
XXI ; R = O; R_1 = Me

* Reduction of the hydroxy lactone (XXIV) with hydriodic acid (in acetic acid) was investigated with a view to prepare santanolide C. However, the major product was the 3β-acetoxy compound (XXVI).

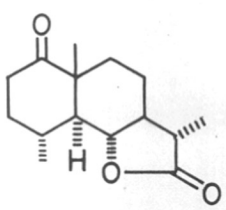
has yielded a mixture of (XXI) and (III). This is further supported by the observations of Geissmann and Ellstad[8] who also obtained a similar mixture of (XXI) and (III) by treating (III) with acetic acid and traces of perchloric acid. These data show that appreciable amount of the β, ɣ-unsaturated ketone (III) is present in equilibrium with the isomeric ketone (XXI). There are precedents in literature[54] for this type of equilibrium. The formation of the required 1-oxo product during the allylic oxidation has been confirmed by hydrogenating the oxidation product and isolating 1-oxosantanolide A (XXXVI), m.p. 118-119°, (ν $CHCl_3$ max 1770 and 1710 cm^{-1}) identical with an authentic sample.[35] The mixture of (XXI) and (III) prepared by a different route* has been already transformed by Honwad and Rao[35] to tauremisin.



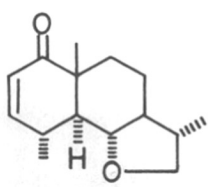
(III)



(XXI)



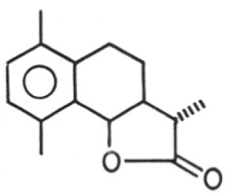
(XXXVI)



(XXXVII)

* this involves oxidation of (XXXVII).

A convenient method has been developed for the preparation of isohyposantonin (XXXVIII) based on dienol-benzene rearrangement.[55] Reduction of santonin with sodium borohydride and treatment of the resulting product with acetic anhydride and sulphuric acid furnished in excellent yield isohyposantonin[56,57] (XXXVIII) identified through its m.p., rotation and elemental analysis.



(XXXVIII)

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

2β-bromo-3-oxo-5,7α(H), 4,6,11β(H)-eudesman-6,13-olide (IX)

To a solution of α-tetrahydrosantonin (X)(3.0 g. obtained by hydrogenation of santonin in the presence of Pd-C catalyst) in chloroform (24 ml) was added dropwise with stirring, a solution of bromine (1.82 g) in chloroform (15 ml) with ice-cooling. After completion of the addition, stirring was continued for 15 minutes, and then a small quantity of ethanol was added. Most of the chloroform was removed under the reduced pressure (temperature of the bath did not exceed 40°), residue was cooled and diluted with ether. Solid which precipitated (3.3732 g) was recrystallised from chloroform-ether to give (IX) melting at 143-144°(decomp). Lit. value[26] m.p. 145-147° (decomp). Mixed m.p. with α-tetrahydrosantonin: 133-136°.

Specific rotation: $(\alpha)_D$ = + 11° (c, 2.15% in chloroform). Lit. value[26] $(\alpha)_D$ = + 9.0° (c, 1.33% chloroform).

IR spectrum (solution in CH_2Cl_2) shows prominent bands at: 3000, 1780, 1725, 1450, 1380, 1180, 1140, 1110, 1020 and 990 cm^{-1}.

3-Oxo-5,7α(H),4,6,11β(H)-eudesm-1-en-6,13-olide (VIII)

Bromocompound (IX) (2.6228 g) was refluxed with purified γ-collidine (25 ml) for 40 hrs in an atmosphere of nitrogen. Reaction mixture was cooled, diluted with ether and the collidine salt (2.2456 g) that separated was filtered off. After washing with 10% HCl and with water, the ether solution was dried and evaporated, leaving a red oil (1.2594 g), which was sublimed under vacuum (130° (bath)/ 0.02 mm) to furnish 64% pure (ε = 5704 at 227 mμ) conjugated ketone (0.8139 g). This was recrystallysed several times from benzene-pet.ether 40-60° to give 97% pure (ε = 8653 at 227.5 mμ)(Lit. value[26] λ_{max} = 227 mμ, ε 8920), material melting at 133-135°. Lit value[26] m.p. 139-140°.

I.R. spectrum (solution in CH_2Cl_2) (p.137) shows prominent bands at: 2960, 1780, 1720, 1687, 1450, 1370, 1226, 1145, 1110, 1010 and 990 cm^{-1}.

1α,2α-Oxido-3-oxo-5,7α(H),1,2,4,6,11β(H)-eudesman-6,13-olide (XV)

To the solution of conjugated ketone (VIII)(0.6598 g) in dioxane (34 ml), 30% hydrogen peroxide (2.5 ml) and 1N NaOH (6.9 ml) were added, the reaction mixture was kept at the room temperature for 24 hrs, diluted with water and extracted with ether. Ether extract was washed with water, dried and evaporated.

Solid residue (0.4922 g) melted at 112-118° and was recrystallised from ethanol two times. U.V. spectrum of recrystallised oxide does not show presence of unreacted conjugated ketone (no absorption at 227 mμ). This material was sublimed under vacuum (150°(bath)/1.35 mm) to give solid melting at 124-127°.

Specific rotation: $(\alpha)_D$ = 120° (c, 5.015% in chloroform).

Optical rotatory dispersion: $[\phi]^{MeOH}_{322\ m\mu}$ + 3140 (first extremum),

$[\phi]^{MeOH}_{270\ m\mu}$ - 3280 (second extremum).

Analysis Found: C, 68.19; H, 7.70. $C_{15}H_{20}O_4$ requires: C, 68.16; H, 7.63%.

I.R. spectrum. (in Nujol; p. 158) shows prominent bands at: 2900, 1780, 1720, 1480, 1390, 1210, 1165, 1125, 1033, 998, 887, 877, 802 and 739 cm^{-1}.

N.M.R. spectrum (p.147) showed signals at 9.02 (3H, singlet, angular CH_3), 8.86, 8.77 and 8.63τ (6H, CH_3 groups at C-11 and C-4) [(the signal at 8.86τ is due to the doublet of CH_3 at C-11; the signal at 8.63τ is due to the doublet at CH_3 at C-4; the intense signal at 8.77τ is due to merger of one of the doublets of CH_3 on C-11 with one of the doublets of CH_3 on C-4)], 6.77τ (2H, H attached to C-1 and C-2) and 6.15τ (1H; broad; H attached to C-6).

Allylic alcohol (XVI)

Keto-oxide (XV) (0.2502 g) was refluxed with 80% hydrazine hydrate (1.35 ml) and isopropylalcohol (5.25 ml)

for 30 min. on the steam bath, kept on the room temperature for 2 hrs, diluted with ice-cold water and extracted with ether. Ether extract on working up furnished 0.0255 g. of gummy material.

I.R. spectrum (smear) shows prominent bands at: 3400, 3000, 1790, 1760, 1670, 1475, 1395, 1300, 1140, 1080, 1020 and 980 cm^{-1}.

Aqueous layer (110 ml) was cooled in ice, acidified by addition of 2N HCl to $p_H \sim 6$, evaporated to dryness and extracted with hot chloroform. Undissolved material was filtered off and filtrate was evaporated leaving residue (0.1723 g) which was chromatographed over alumina (g. III; 7 g). Ethanol eluted fraction furnished thick oil (0.1552 g).

I.R. spectrum (liq. film) shows prominent bands at: 3390, 2970, 1780, 1670, 1460, 1390, 1055, 1035 and 1000 cm^{-1}.

This material was sublimed under vacuum (temperature up to 200°(bath)/0.3 mm) and obtained substance was kept in cold for several days but no crystalline material was obtained.

3β-Acetoxy-4,5α(H),6,11β(H)-eudesman-6,13-olide (XXVI)

Santonin (5.0122 g) in acetic acid (150 ml) was stirred with Pt-C catalyst (0.3820 g) in hydrogen for 24 hrs at 25° and 727 mm Hg. It absorbed 1655 ml of hydrogen. Catalyst was filtered off. From filtrate the solvent was

removed by distillation under reduced pressure (water aspirator), residue was treated with ether (50 ml), undissolved solid was removed and ethereal solution evaporated. Residue (6.5880 g) was heated on the steam bath with pyridine (5.5 ml) and acetic anhydride (6 ml) for 2 hrs. After removal of the solvents, the crude acetate was obtained in 90% yield and recrystallised from ethanol to give needles melting at 196-198°. Lit value[36] m.p. 199-200°.

Specific rotations: $(\alpha)_D$ = + 13.8° (c, 0.76% in chloroform). Lit. value $(\alpha)_D^{36}$ + 15.4° (c, 0.72% in chloroform).

I.R. spectrum (in Nujol; p.144) shows prominent bands at: 3000, 1755, 1725, 1465, 1365, 1250, 1130, 1030 and 990 cm^{-1}.

N.M.R. spectrum (in chloroform; p.149) showed signals at: 9.08, 8.95, 8.85 and 8.74 τ (9H, due to CH_3 on C-4, angular CH_3 and CH_3 attached to C-11) (doublet centred at 8.80 τ is due to CH_3 on C-11; intense signal at 8.95 τ is due to merger of singlet of angular CH_3 and one of the doublets of CH_3 on C-4; the other part of doublet due to CH_3 on C-4 is at 9.08 τ), 7.97 τ (3H, singlet; $CH_3-\overset{O}{\overset{\|}{C}}-O$) signals (broad) centred at 6.0 τ (1H, H attached to C-6) and signals (broad) centred at 5.13 τ (1H, H attached to C-3).

3β-Hydroxy-4,5α(H),6,11β(H)-eudesman-6,13-olide (XXIV)

Acetate (XXVI) (1.0164 g) was refluxed for 2 hrs with KOH (0.5059 g) in methanol (25 ml), cooled in ice, acidified by

addition of conc. sulphuric acid and extracted with chloroform continuously for 24 hrs. Chloroform extract was washed with water, dried and evaporated. The residue after the recrystallisation from ethanol ~~dried and evaporated~~ gave the required hydroxy compound in 70% yield. Melting point: 102-103°. Lit. value[36] m.p. 108-110°.

Specific rotation: $(\alpha)_D$ = + 37.6° (c, 0.85% in ethanol). Lit. value[36] $(\alpha)_D$ = + 36° (c, 0.95 in ethanol).

I.R. spectrum (in Nujol; p.143) shows prominent bands at: 3450, 3000, 1775, 1465, 1380, 1220, 1035, 1050, 1030 and 990 cm^{-1}.

N.M.R. spectrum (in chloroform; p.149) showed signals at: 9.08, 8.95 and 8.72 τ (9H, due to CH_3 on C-4, angular CH_3 and CH_3 attached to C-11). (The doublet centred at 8.78 τ can be assigned to C-11, CH_3 on the basis of comparison with a number of lactones carrying CH_3 at C-11; the intensity of the signal at 8.95 τ suggests that this is due to the merger of singlet of angular CH_3 and one of the doublet signals of CH_3 attached to C-4; the signal at 9.02 τ is due to one of the doublet signals of CH_3 attached to C-4), 7.42 τ (sharp; singlet due to -OH at C-3; this signal disappears after equilibration with D_2O) and 5.80-6.40 τ (2H, broad, due to H attached to C-3 and C-6).

Action of p-toluene-sulphonic acid on hydroxy lactone(XXIV)

Hydroxy lactone (XXIV) (0.2076 g) was refluxed for 2 1/2 hrs with acetic acid (3 ml) in the presence of p-toluenesulphonic acid (0.0404 g). The reaction mixture was diluted with ether, washed with cold sodium carbonate solution and water, and dried. Residue (0.1789 g) obtained after evaporation, was recrystallised from ethanol to furnish the acetate (XXVI) identified by mixed m.p. with an authentic sample (192-196°; lit.value[36] m.p. 199-200°) and IR spectrum.

Attempted dehydration of hydroxy lactone (XXIV) with p-toluenesulphonyl chloride and sulphur dioxide

A solution of hydroxy lactone (0.5358 g), p-toluene-sulphonyl chloride (1.3190 g) and dimethylformamide (10 ml) was cooled to 10° and dry collidine (2 ml) was added. This solution was treated with saturated solution of sulphur dioxide in dimethylformamide (2 ml) cooled to 10°, kept at the room temperature for 30 minutes, again cooled to 10°, diluted with water and extracted with ether. Ether extract was washed with N/2 HCl and with water, dried and evaporated. Residue (0.4757 g) melted at 195°.

Analysis: Found C, 68.47; H, 8.7. $C_{16}H_{24}O_4$ (XXXIV) requires: C, 68.57; H, 8.57%.

I.R. Spectrum (in Nujol) shows prominent bands at: 2950, 1780, 1720, 1450, 1375, 1190, 1110, 990, 935 and 910 cm^{-1}.

Ester (0.1084 g), m.p. 195°, was saponified by refluxing for 2 1/2 hrs with KOH (0.0738 g) in methanol(10ml), diluted with water, methanol was evaporated, residue was cooled in ice, acidified by addition of conc. sulphuric acid and extracted with ether. Ethereal extract was washed with cold NaOH solution and water, dried and evaporated to give the starting hydroxy lactone (XXIV) (0.0501 g), which was identified by its IR spectrum and TLC behaviour, identical to that of (XXIV) (both show single spots, R_f value = 0.225).

N.M.R. spectrum (in chloroform;) showed signals at: 9.03, 8.90, 8.83 and 8.17 τ (9H due to CH_3 on C-4, angular CH_3 and CH_3 on C-11) (doublet centred at 8.77 τ is due to CH_3 on C-11; intense signal at 8.90 τ is due to merger of singlet of angular CH_3 and one of the doublet signals due to CH_3 on C-4; the remaining part of the doublet due to CH_3 on C-4 appears at 9.03 τ).

Attempted reduction of hydroxy lactone (XXIV) with hydriodic acid

To a mixture of hydroxy lactone (XXIV) (0.260 g), 5.5 ml of acetic anhydride and 5.5 ml of glacial acetic acid, was added dropwise 27% HI (18.3 ml). It was refluxed for 40 minutes, cooled, poured into ice-cold water, neutralised by addition of solid sodium carbonate and extracted with ether. Ether extract was washed with dilute NaOH solution and water, dried and evaporated leaving the residue (0.2276 g) which was sublimed under vacuum (temperature up to 195°(bath)/5 mm),

and compared by T.L.C. with the starting hydroxy lactone (XXIV), acetate (XXVI) and santanolideC(II). T.L.C. studies showed that it contains the acetate (XXVI) and unreacted hydroxy lactone (XXIV) but does not contain santanolide C (II). This conclusion was confirmed by the IR spectrum which shows bands for hydroxy lactone (3580 cm^{-1}) and for acetate (1725 and 1250 cm^{-1}).

Tosylate of 3β-hydroxy-4,5α(H), 6,11β(H)-eudesman-6,13-olide (XXXI)

Hydroxy lactone (XXIV) (0.2659 g) and p-toluenesulphonyl chloride (0.4159 g) in dry pyridine (4 ml) were heated at 48-53° for 45 hrs, reaction mixture was poured into ice cold sodium carbonate solution (50 ml) and extracted with ether. Ether extract was washed with cold 1N HCl and with water, dried and evaporated. Residue (0.3284 g) was recrystallised from ethanol. Melting point: 163-169°. Lit.value[21] m.p. 168-169°.

Specific rotation: $(\alpha)_D$ = + 22° (c, 3.015% in chloroform). Lit.value[21] $(\alpha)_D$ = + 20° (c, 1.7 in chloroform).

Analysis: Found: C, 65.12; H, 7.14; S, 8.34. $C_{22}H_{30}SO_5$ requires: C, 65.01; H, 7.44%, 7.87%.

I.R. spectrum (in Nujol) shows prominent bands at: 3000, 1675, 1475, 1380, 1190, 995, 950, 918, 870, 848 and 818 cm^{-1}.

5α(H),6,11β(H)-eudesm-3-en-6,13-olide(XX)

Preparation of potassium tert.-butoxide and dimethylsulphoxide reagent (KtBD): potassium (0.30 g was dissolved in

dry tert. butanol (7 ml) and refluxed for 2 hrs. Solvent was removed under the reduced pressure, dimethylsulphoxide (7.5 ml) was added and mixture was stirred until it formed the uniform solution.

Tosyl ester (XXXI) (0.2061 g) dissolved in dry benzene (3.5 ml), was treated with KtBD reagent (prepared as above), stirred at room temperature (in the dark) for 47 hrs, diluted with water, cooled in ice, acidified by addition of conc. sulphuric acid and extracted with ether. Ether extract was washed with water, dried and evaporated. Residue was sublimed under vacuum (temp. up to 200°(bath)/0.5 mm) to give 0.1016 g. of a white solid $(\alpha)_D$ = + 120° (c,1.67 in chloroform), which was chromatographed over alumina, gr.II (5 g). The fraction eluted with mixture of pet.ether 40-60° and benzene (1:1) $(\alpha)_D$ = + 116.8° (c, 1.67 in chloroform) was composed predominantly of (XX) as its I.R. spectrum was in good agreement with that of an authentic sample.

Analysis: Found: C, 77.18; H, 9.25. $C_{15}H_{22}O_2$ requires: C, 76.88; H, 9.46%.

I.R. spectrum (solution in CS_2; p.142) shows prominent bands at: 3000, 1800, 1680, 1380, 1330, 1240, 1180, 1140, 1120, 1030 and 1000 cm^{-1}.

N.M.R. spectrum (in chloroform; p.148) of elimination product was comparable with that of an authentic sample of Δ^3-santenolide (XX). The only noticeable difference between the N.M.R. spectra of the above elimination product and authentic (XX) is the presence of a signal at 8.98τ in the elimination product.

Assuming that the signal at 8.98τ is part of a doublet due to CH_3 on C-4 of (XIX), the composition of elimination product can be calculated. The area under the N.M.R. signals of elimination product in the region 8.65-9.2τ (due to CH_3-C) shows the presence of 6.5 protons, while the authentic sample of (XX) shows the presence of 6.0 protons, and (XIX) shows the presence of 9.0 protons. Hence the elimination product is a mixture of (XX) (84%) and (XIX) (16%).

N.M.R. spectrum of authentic sample of (XX)* showed signals at 9.06τ (3H, angular CH_3), 8.83τ (3H, doublet: J = 7.0 c.p.s. CH_3 attached to C-11), 8.18τ (3H, CH_3 attached to C-4), 6.20 (1H, broad, H attached to C-6) and 4.66τ (1H, vinyl proton at C-3).

Benzoate of 3β-hydroxy-4,5α(H),6,11β(H)-eudesman-6,13-olide (XXXIII)

Hydroxy lactone (XXIV) (0.2170 g) in dry pyridine (0.8 ml) was cooled in ice and mixed with benzoyl chloride (0.25 ml). Reaction mixture was allowed to stand at the room temperature for 24 hrs, then added to the cold water(7 ml), allowed to stand at the room temperature for another 8 hrs, diluted with more water and extracted with ether. Ether extract was washed with cold sodium carbonate solution, cold dilute sulphuric acid, and with water, dried and evaporated.

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* The sample used for the N.M.R. spectrum was prepared by Dr. A.M. Shaligram.

Residue (0.3058 g) was recrystallised from ethanol to furnish the benzoate, m.p. 184-187°.

Specific rotation: $(\alpha)_D$ = + 67.5° (c, 3.0% in chloroform).

Analysis: Found: C, 73.60; H, 8.04. $C_{22}H_{28}O_4$ requires: C, 74.13; H, 7.92%.

I.R. spectrum (in Nujol) shows prominent bands at: 2950, 1760, 1720, 1600, 1450, 1375, 1310, 1275, 1105, 1065, 1020, 990 and 713 cm^{-1}.

N.M.R. spectrum (in chloroform; ~~ϕ~~.) shows signals at: 8.92; 8.88, 8.83 and 8.71τ (9H due to CH_3 attached to C-4, angular CH_3 and CH_3 attached to C-11), the signal at 8.71τ is due to one of the doublet signals of CH_3 at C-11; the signal at 8.92τ is due to one of the doublet signals of CH_3 at C-4; the comparatively intense signal at 8.83τ is due to merger of one of the doublet signals of CH_3 at C-11 and one of the doublet signals of CH_3 at C-4; intensity of the signal at 8.88τ suggests that it is exclusively due to the angular CH_3 group).

4,5α(H),6,11β(H)-eudesm-2-en-6,13-olide (XIX)

Benzoyl ester (0.2020 g) was heated at 350° for 45 minutes in an atmosphere of nitrogen, cooled, residue dissolved in chloroform and the solution combined with that obtained by washing the condenser with chloroform. Combined chloroform solutions were washed with cold sodium carbonate solution and with water, dried and evaporated. Residue (0.1466 g)

was sublimed under vacuum (temperature up to 185° (bath)/ 0.2 mm) and obtained solid recrystallised from pet. ether 60-80° to furnish the lactone (XIX) m.p. 107-108°, Lit. value[36] m.p. 107-108°.

Specific rotation: $(\alpha)_D$ = +128° (c, 1.725% in chloroform). Lit. value[36] $(\alpha)_D$ = + 98.6° (c, 0.55% in chloroform).

Analysis: Found: C, 77.34; H, 9.34. $C_{15}H_{22}O_2$ requires: C, 76.88; H, 9.46%.

I.R. spectrum (solution in CS_2; p.140) shows prominent bands at: 3000, 1800, 1375, 1330, 1240, 1210, 1180, 1150, 1105, 1075, 1025, 1000 and 720 cm^{-1}.

U.V. spectrum (in ethanol) λ max. at 214 mμ (ε value 787).

N.M.R. spectrum (p.147) shows signals at: 8.98, 8.93, 8.88 8.82 τ (9H, due to angular CH_3, CH_3 attached to C-4 and CH_3 attached to C-11) (the doublet centred at 8.88τ is due to CH_3 attached to C-11; the intense signal at 8.98τ is due to merger of singlet due to angular CH_3 and one of the doublets of CH_3 attached to C-4; the remaining part of doublet due to CH_3 at C-4 appears at 8.88τ), 6.13τ (broad, 1H, H attached to C-6), 4.40τ (2H, olefinic protons at C-2 and C-3). The comparatively weak signal at 9.10τ may be due to an impurity (Δ^3-santenolide?).

4,5,11α(H),6β(H)-eudesman-6,13-olide (santanolide C)(II)

Unsaturated lactone (XIX) (0.1268 g) in acetic acid (5 ml) was stirred with Pt-C catalyst (0.0152 g) in hydrogen

for 2 hrs at 27° and 715 mm Hg. It absorbed 32 ml of hydrogen. Catalyst was filtered off, most of the solvent was removed by distillation under reduced pressure, residue was dissolved in ether, washed with sodium carbonate solution and water, dried and evaporated. Residue was sublimed under vacuum (temp. up to 160°(bath)/1.5 mm) to give santanolide C (0.1163 g), which after recrystallisation from pet.ether 60-70° had m.p. 147-48°. Lit. value[7] m.p. for santanolide C: 154°. Mixed m.p. with an authentic sample of santanolide C: 148-153°.

Specific rotation: $(\alpha)_D$ = + 62° (c, 1.95 in chloroform). Lit. value[7] $(\alpha)_D$ = +54.8°.

I.R. spectrum (in Nujol) shows prominent bands at: 3000, 1800, 1475, 1380, 1190, 1160, 1135 and 1000 cm^{-1}. (It agrees with the I.R. spectrum of an authentic sample).

T.L.C. Santanolide C (m.p. 147-148°), prepared as described above, was compared with an authentic sample. Both have shown identical R_f values (0.66).

2α,3α-Oxido-4,5,7α(H), 2,3,6,11β(H)-eudesman-6,13-olide(XXXII)

Δ^2-Santenolide (XIX) (0.2000 g) in chloroform (1 ml) was treated for 48 hrs at 0° with 0.7N chloroform solution of perbenzoic acid (3.2 ml), washed with 5% solution of KI, 5% solution of sodium thiosulphate, solution of sodium carbonate and water, dried and chloroform evaporated. Residue (0.2120 g) was recrystallised from ethanol to furnish the oxide (XXXII) m.p. 145-153°.

Specific rotation: $(\alpha)_D$ = + 101° (c, 2.07 in chloroform). One part of this substance was sublimed under vacuum (140° (bath)/0.5 mm) and submitted for elemental analysis.

Analysis: Found: C, 72.11; H, 8.60. $C_{15}H_{22}O_3$ requires: C, 71.97; H, 8.60%.

I.R. spectrum (in Nujol; p.145) shows prominent bands at: 3000, 1800, 1485, 1395, 1218, 1170, 1040 and 1005 cm^{-1}.

Hydrogenation of epoxide (XXXII)

Epoxide (XXXII) (0.1316 g) in acetic acid (7 ml) was stirred with Pt-C catalyst (0.0632 g) in hydrogen for 22 hrs at 26° and 710 mm Hg. Catalyst was filtered off, filtrate was poured into ice cold NaOH solution and extracted with ether. Ether extract was washed with water, dried and evaporated leaving the residue (0.0315 g), which was proved (by its I.R. spectrum and melting point) to be the starting oxide.

Mixture of 1-oxo-5,7α(H), 6,11β(H), 4ξ(H)-eudesm-2-en-6,13-olide (XXI) and 1-oxo-5,7α(H),6,11β(H)-eudesm-3-en-6,13-olide (III)

A solution of unsaturated lactone (XIX) (0.7836 g) and sodium dichromate (1.7130 g) in acetic acid (30 ml) was heated at 100° for 6 hrs in an atmosphere of nitrogen. Excess of dichromate was decomposed by addition of ethanol(1 ml) to the hot solution, cooled, diluted with water and extracted with ether. Ether extract was washed with sodium carbonate solution and water, dried and evaporated. Obtained 0.5555 g. as residue.

I.R. spectrum (in Nujol) shows prominent bands at: 2950, 1775, 1725, 1665, 1450, 1370, 1200, 1145, 1110 and 990 cm^{-1}.

U.V. spectrum (in ethanol): Max. at 235 mμ (ε value 4390). Lit. value[8] for the mixture of (XXI) and (III): Max. at 220 mμ (ε value 4240).

1-Oxo-5,7α(H),4,6,11β(H)-eudesman-6,13-olide (XXXVI)

Experiment I

Mixture of (XXI) and (III) (0.075 g) in acetone (10 ml) was stirred with 5% Pd-C catalyst (0.1028 g) in hydrogen for 17 hrs at 29° and 712 mm Hg. It absorbed 5 ml of hydrogen. Catalyst was filtered off. Removal of the solvent from the filtrate furnished 0.0697 g. of solid, which was recrystallised from ethanol to give (XXXVI), m.p. 118-119°. Lit. value[35] 117-119°.

Analysis: Found: C, 71.85; H, 8.81. $C_{15}H_{22}O_2$ requires: C, 71.96; H, 8.66%.

I.R. spectrum (in Nujol) shows prominent bands at: 2950, 1770, 1710, 1450, 1380, 1330, 1200, 1010 and 990 cm^{-1}.

Experiment 2

Mixture of (XXI) and (III) (0.550 g) in acetic acid (22.5 ml) was stirred with Pt-C catalyst (0.200 g) in hydrogen for 22 hrs at 28° and 710 mm Hg. Catalyst was filtered off, from filtrate the solvent was removed by distillation under

reduced pressure (water aspirator), residue was poured into ice-cold sodium carbonate solution and extracted with ether. Ether extract was washed with water, dried and evaporated. Residue (0.3913 g) was dissolved in acetone (50 ml), oxidised by addition of Jones reagent (1 ml), excess of Jones reagent was destroyed by addition of ethanol (1 ml), diluted with water and extracted with ether. Ether extract on working up gave solid (0.3030 g), which after recrystallisation from ethanol furnished crystals (0.0606 g) identified as santanolide C, by its melting point (134-138°) and its I.R. spectrum (identical to that of an authentic sample of santanolide C).

Solid (0.2111 g) obtained from the mother liquor was chromatographed over alumina, gr.II (6 g). It was eluted with pet.ether 40-60° and subsequently with a mixture of benzene and pet.ether 40-60° (1:1). Elution with mixture of benzene and pet.ether 40-60° (1:1) furnished solid which was sublimed under vacuum (temperature up to 190°(bath)/0.5 mm) and recrystallised from benzene-pet.ether 60-80° to give 1-oxo-santanolide A (XXXVI) melting at 113-115°. Lit.value[35] m.p. 117-119°.

Analysis: Found: C, 71.60; H, 8.84. $C_{15}H_{22}O_3$ requires: C, 71.96; H, 8.66%.

I.R. spectrum (solution in chloroform; p.146) shows prominent bands at: 2950, 1770, 1710, 1450, 1380, 1330, 1180, 1010, 990 and 940 cm^{-1}.

Isohyposantonin (XXXVIII)

To a suspension of santonin (2.0605 g) in methanol (60 ml) was added sodiumborohydride (1.1106 g) in small portions and it was allowed to stand overnight when a clear solution resulted. The excess of $NaBH_4$ was destroyed by careful addition of acetic acid (2 ml), solvent was removed in vacuo, residue was diluted with water and extracted with ether. Ether extract was washed with water, dried and evaporated. Residue (2.3222 g) was dissolved in warm acetic anhydride (50 ml), solution was cooled to the room temperature and solution of conc. sulphuric acid (0.4 g) in acetic anhydride (4 ml) was added dropwise. After the period of 3 hrs conc. sulphuric acid (0.2 g) in acetic anhydride (2 ml) was added, it was allowed to stand at the room temperature overnight, then poured into ice cold 45% KOH solution (110 ml) and extracted with ether. Ether extract was washed with water, dried and evaporated to give isohyposantonin (1.8810 g), m.p. 162-163°, $(\alpha)_D$ = - 72.2°. To obtain analytical sample of isohyposantonin, chromatography over alumina, gr.III (60 g) was done, and fraction eluted with benzene-pet.ether 40-60° (1:1 mixture) was recrystallised from ethanol to give pure isohyposantonin, m.p. 167-169°. Lit. value[56] m.p. 168.5°.

Specific rotation: $(\alpha)_D$ = - 71° (c, 1.61% in benzene). Lit. value[56] $(\alpha)_D$ = + 70.3°.

Analysis: Found: C, 77.96; H, 8.04. $C_{15}H_{18}O_2$ requires: C, 78.23; H, 7.88%.

I.R. spectrum (solution in CH_2Cl_2) shows prominent bands at: 2950, 1760, 1420, 1260, 1220, 1165, 982, 950, 895, 818, 764 and 710 cm^{-1}.

U.V. spectrum (in ethanol). λ max. at 270 mμ (ε value 1063).

N.M.R. spectrum (in chloroform; ~~ref.~~) shows signals at: 8.60τ (doublet; J = 7 c.p.s.) due to CH_3 attached to C-11, 7.70τ and 7.57τ due to CH_3 groups attached to the aromatic ring.

SUMMARY

The major product obtained during the hydrogenation of santonin in acetic acid in the presence of platinum on charcoal catalyst is shown to be 3β-hydroxy-4,5α(H), 6,11β (H)-eudesman-6,13-olide, m.p. 102-103°, $(\alpha)_D$ + 37.6°. For this compound Cocker and McMurry have previously assigned α-orientation for hydroxyl group. It is now suggested that the hydroxy lactone has a β-oriented hydroxyl group at C-3. Elimination reaction of this hydroxy lactone and its esters have been studied. Improved methods for preparation of 4,5α(H), 6,11β(H)-eudesm-2-en-6,13-olide, 5α(H), 6,11β(H)-eudesm-3-en-6,13-olide; santanolide C and isohyposantonin have been developed. Oxidation of 4,5α(H), 6,11β(H)-eudesm-2-en-6,13-olide with sodium dichromate in acetic acid furnished a mixture of starting material and keto-lactones: 1-oxo-5,7α(H),6,11β(H),4 (H)-eudesm-2-en-6,13-olide, and 1-oxo-5,7α(H), 6,11β(H)-eudesm-3-en-6,13-olide (which has been converted into tauremisin by Rybalko). Hydrogenation of this mixture of ~~this~~ keto-lactones followed by chromatography and repeated recrystallisations furnished 1-oxo-5,7α (H),4,6,11β(H)-eudesman-6,13-olide. 1α,2α-Oxido-3-oxo-5,7α (H), 1,2,4,6,11β(H)-eudesman-6,13-olide, a potential intermediate for the synthesis of tauremisin has been prepared.

REFERENCES

1. T. Kawatani and T. Takeuchi, J. Pharm.Soc.(Japan), 74, 793 (1954).

2. W.G. Dauben, J.S.P. Schwarz, W.K. Hayes and P.D. Hance, J.Am.Chem.Soc., 82, 2239 (1960).

3. J.D.M. Asher and G.A. Sim, Proc. Chem. Soc., 111(1962).

4. D.H.R. Barton, J.E.D. Levisalels and J.T. Pinhey, J. Chem.Soc., 3472 (1962).

5. "The Terpenes" by Sir J. Simonsen and D.H.R. Barton, Cambridge University Press (1952), Vol. III, p. 322.

6. W.G. Dauben, W.K. Hayes, J.S.P. Schwarz and J.W. McFarland, J. Am.Chem.Soc., 82, 2232 (1960).

7. K.S. Rybalko and L. Dolejs, Coll. Czech.Chem.Comm., 26, 2909 (1961).

8. T.A. Geissman and G.A. Ellestad, J. Org. Chem., 27, 1855 (1962).

9. M. Suchy, Coll. Czech. Chem. Comm., 27, 2925 (1962).

10. W. Herz and N. Viswanathan, J. Org. Chem., 29, 1022 (1964).

11. W. Herz, G. Hogenauer and A.R. de Vivar, J. Org. Chem., 29, 1700 (1964).

12. S. Matsuda and T.A. Geissman, Tetrahedron Letters, 2013 (1967).

13. S. Matsuda and T.A. Geissman, Tetrahedron Letters, 2159 (1967).

14. H. Minato and M. Ishikawa, J. Chem. Soc. (C), 423(1967).

15. A.R. de Vivar and H. Jimenez, Tetrahedron, 21, 1741 (1965).

16. E. Kurosawa, M. Izawa, K. Jamamoto, T. Masamune and T. Irie, Bull. Chem. Soc. (Japan), 39, 2509(1966).

17. O. Kovacs, V. Herout, M. Horak and F. Sorm, Coll. Czech. Chem. Comm., 21, 225 (1956).

18. A.S. Rao, G.R. Kelkar and S.C. Bhattacharyya, Tetrahedron, 9, 275 (1960).

19. A.S. Rao, A. Paul, Sadgopal and S.C. Bhattacharyya, Tetrahedron, 13, 319 (1961).

20. A.M. Shaligram, A.S. Rao and S.C. Bhattacharyya, Tetrahedron, 18, 969 (1962).

21. H. Ogura, J. Org. Chem., 25, 679 (1960).

22. G.D. Joshi, M.V. Kadival, S.N. Kulkarni and S.C. Bhattacharyya, Tetrahedron, 23, 1985 (1967).

23. M. Nakazaki and H. Arakawa, Proc. Chem. Soc., 151 (1962).

24. J.D.M. Asher and G.A. Sim, Proc. Chem. Soc., 335(1962).

25. C. Djerassi, D.H. Williams and B. Berkoz, J. Org. Chem., 27, 2205 (1962).

26. M. Yanagita and A. Tahara, J. Org. Chem., 20, 959(1955).

27. J.B. Hendrickson and T.L. Bogard, J. Chem. Soc., 1678 (1962).

28. E.W. Garbisch, Jr., J. Org. Chem., 30, 2109 (1965); E. W. Warnhoff and D.R. Marshall, J. Org. Chem., 32, 2000 (1967).

29. G.H. Kulkarni, A. Paul, A.S. Rao, G.R. Kelkar and S.C. Bhattacharyya, Tetrahedron, 12, 178 (1961).

30. K.W. Gopinath, T.R. Govindachari, P.C. Parthasarathy, N. Viswanathan, D. Arigoni and W.C. Wildman, Proc. Chem. Soc., 446 (1961).

31. G. Stork and W.N. White, J. Am. Chem. Soc., 78, 4604 (1956).

32. C. Djerassi, W. Klyne, T. Norin, G. Ohloff and E. Klein, Tetrahedron, 21, 163 (1965).

33. P. Striebel and Ch. Tamm, Helv. Chim. Acta, 37, 1094 (1954).

34. E. Klein and G. Ohloff, Tetrahedron, 19, 1091(1963).

35. V.K. Honwad and A.S. Rao, Ph.D. Thesis submitted by Dr. V.K. Honwad to the University of Poona (1966); V.K. Honwad, E. Siskovic and A.S. Rao, Tetrahedron, 23, 1273 (1967).

36. W. Cocker and T.B.H. McMurry, J. Chem.Soc., 4549(1956).

37. H.J. Ringold and G. Rosenkranz, J. Org. Chem., 22, 602 (1957).

38. W.G. Dauben, E.J. Blanz, Jr., J. Jiu and R. Micheli, J. Am.Chem.Soc., 78, 3752 (1956).

39. D.H.R. Barton, J. Chem. Soc., 1027 (1953).

40. S. Julia, B. Decuveleare, J.P. Lavaux, C. Movtonnier and P. Simon, Bull. Soc. Chim. France, 1223(1963).

41. E.L. Eliel, M.H. Gianni and Th. H. Williams, Tetrahedron Letters, 741 (1962).

42. R.E. Counsell, Tetrahedron, 15, 202 (1961).

43. F.C. Chang and R.T. Blickenstaff, J. Am. Chem. Soc., 80, 2906 (1958).

44. F.C. Chang, N.F. Wood and W.G. Holton, J. Org. Chem., 30, 1718 (1965).

45. G.G. Hazen and D.W. Rosenburg, J. Org. Chem., 29, 1930 (1964).

46. N.S. Bhacca and O.H. Williams: Application of N.M.R. spectroscopy in organic chemistry, Holden-Day Inc. (1964),p. 77.

47. F.C. Chang and N.F. Wood, Steroids, 4 (1), 55 (1964).

48. K. Yamakawa, J. Org. Chem., 24, 897 (1959).

49. J.A. Mills, J. Chem. Soc., 4976 (1952).

50. T.R. Ames, J.L. Beton, A. Bowers, T.G. Halsall and E.R.H. Jones, J. Chem. Soc., 1905 (1954).

51. R.C. Fuson and H.P. Wallingford, J. Am. Chem. Soc., 75, 5950 (1953).

52. B.R. Davis and T.G. Halsall, J. Chem. Soc., 1833(1962).

53. E.J. Corey and J.J. Ursprung, J. Am. Chem. Soc., 78, 183 (1956).

54. K.G. Lewis and G.J. Williams, Tetrahedron Letters, 4573 (1965).

55. M. Jevnik Gentles, J.B. Moss, H.L. Herzog and E.B. Herchberg, J. Am. Chem.Soc., 80, 3702 (1958).

56. same as 5, p. 252.

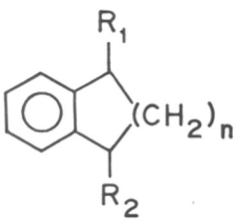
57. D.H.R. Barton, J. Org. Chem., 15, 466 (1950).

chapter II

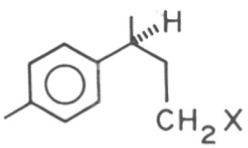
transformations of (+) ar-turmerone

Compounds of the type (I) having an alicyclic ring attached to the vicinal carbon atoms of a benzene ring are widely distributed in nature.* This and certain other factors prompted us to prepare some bicyclic compounds, with one aromatic ring and one alicyclic ring as shown in formula (I).

Recently a number of optically active compounds of the type (II) having only one asymmetric carbon atom have been prepared by Honwad and Rao[2] in connection with their studies on the absolute configuration of (+) ar-turmerone (III) and (+)-α-curcumene (IV). It has been pointed out that in the above series (II), all compounds having the



I



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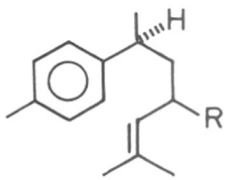

III ; R = O

IV ; R = H_2

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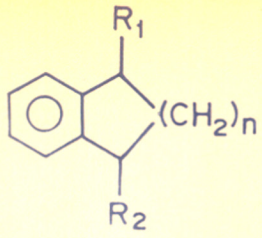
* The O.R.D. and C.D. curves of compounds containing benzene ring as chromophore have been reviewed recently by Crabbe and Klyne.[1] A number of naturally occurring compounds of the type (I) are mentioned in this review. Particular mention may be made of lignans having the phenyltetralin skeleton; O.R.D. curves of more than a hundred lignans have been measured by Klyne's group.



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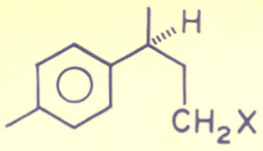

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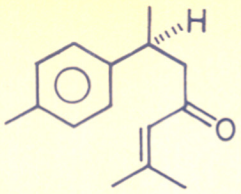

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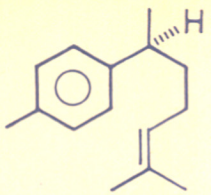

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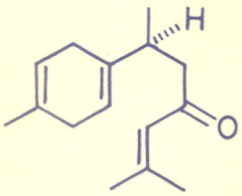

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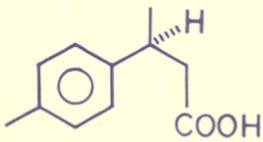

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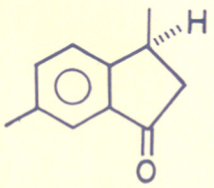

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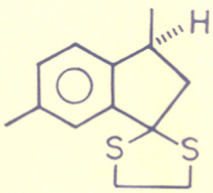

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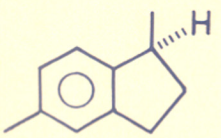

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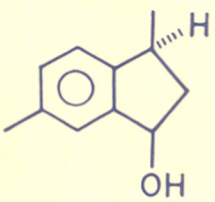

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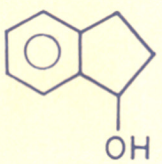
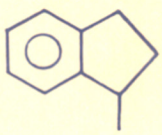


(XI)



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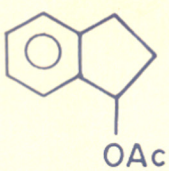

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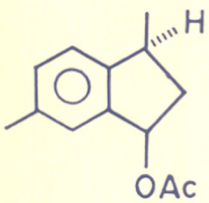

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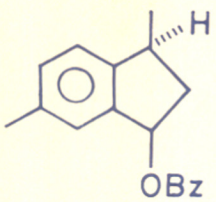

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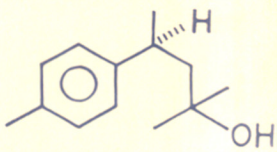

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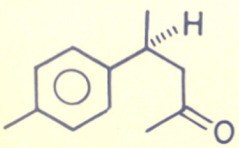

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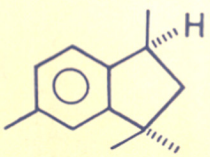

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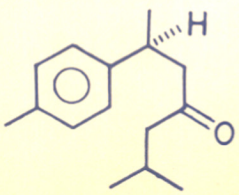

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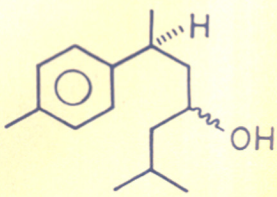

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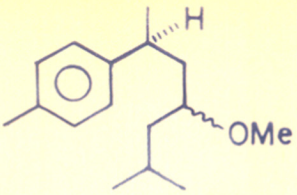

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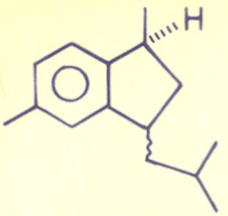

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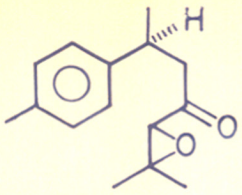

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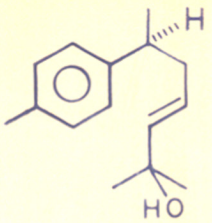

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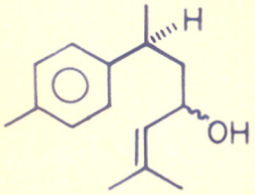

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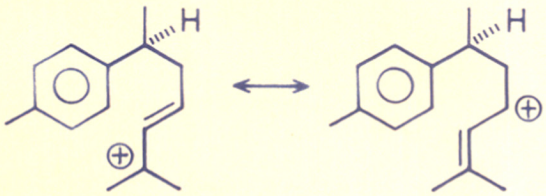
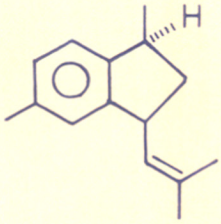


(XXVIa) (XXVIb)



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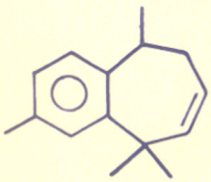

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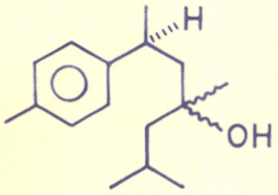

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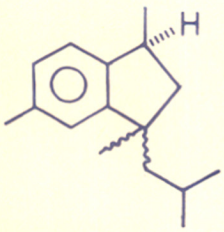

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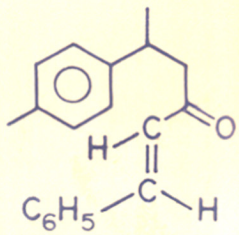

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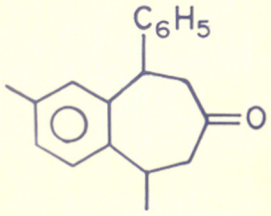

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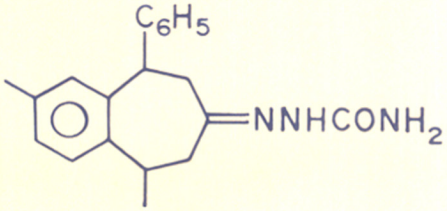

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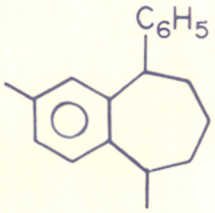

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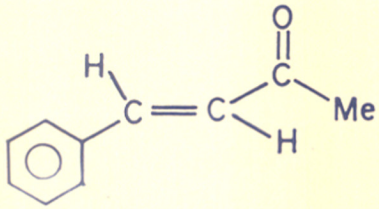

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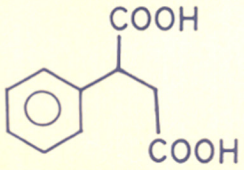

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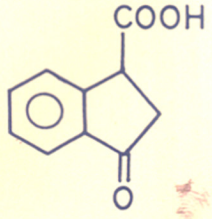

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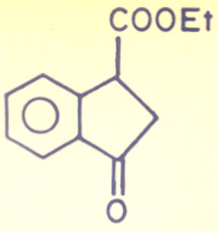

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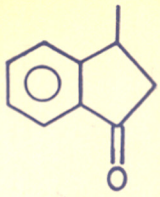

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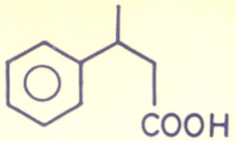

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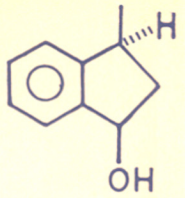

(XLI)

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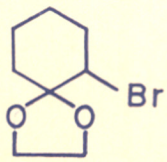

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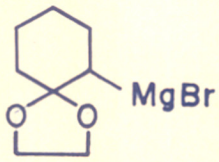

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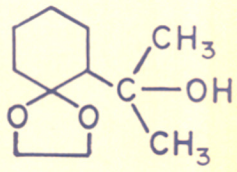

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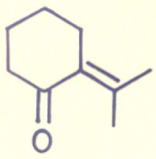

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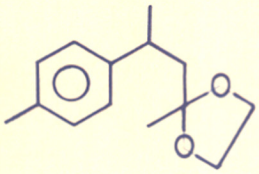

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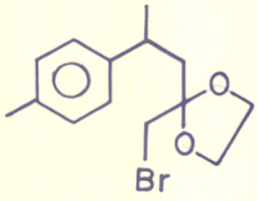

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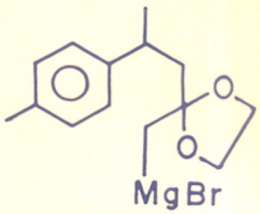

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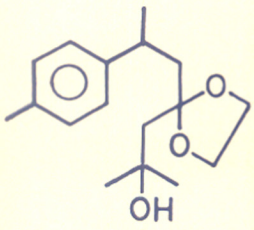

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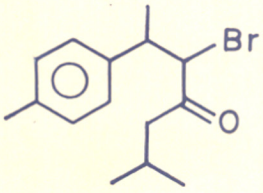

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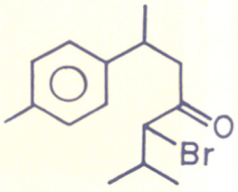

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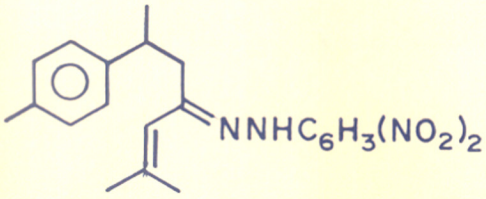

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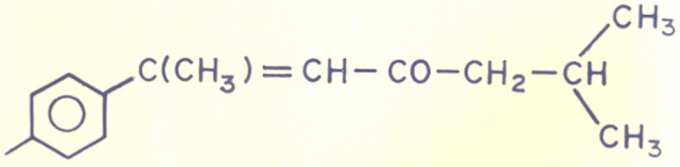

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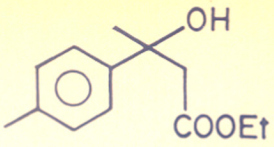

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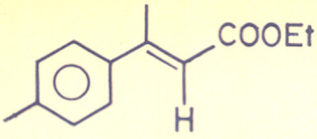

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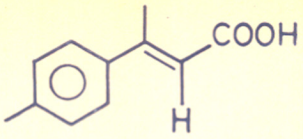

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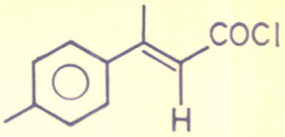

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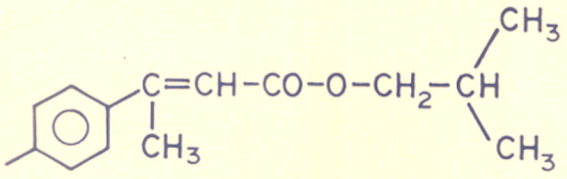

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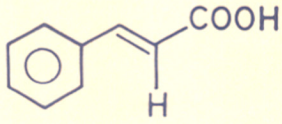

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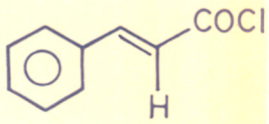

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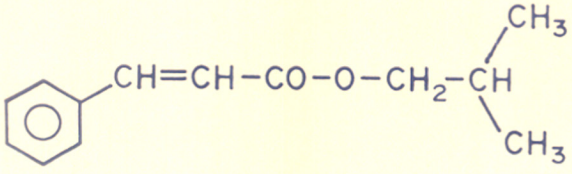

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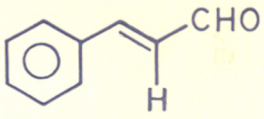

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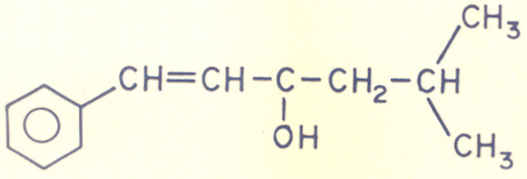

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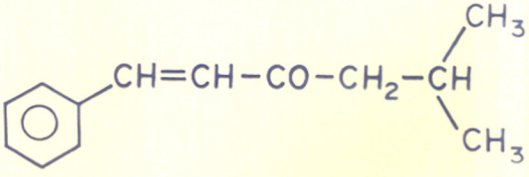
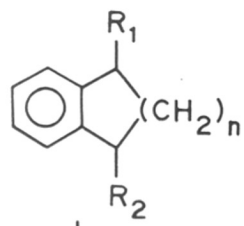


(LXV)

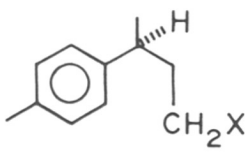
S-configurations are dextrorotatory in agreement with the predictions based on the principles of conformational asymmetry.[3]

A flexible chain compound will generally have a relatively small rotation because its molecules can assume many conformations with different and opposed rotatory powers. The relatively large rotations of ring compounds has been ascribed to their near rigidity which allows a display of the full rotatory powers of their asymmetric conformations.[3] Hence it was anticipated that the rotation of the bicyclic compounds (I) (especially when 'n' is small) could be different from that of the monocyclic compounds (II).

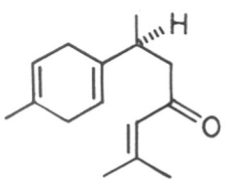
Turmerone (V), the major constituent of turmeric oil was oxidised by Jones reagent[4] to ar-turmerone, which furnished the (+) acid (VI)[5] on ozonolysis. The (+) acid (VI) was cyclised to the ketone (VII) [(ν_{max} 1720 cm^{-1} due to -C=O group



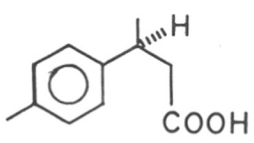
I



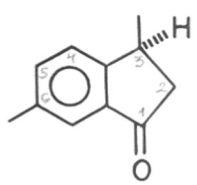
II



V

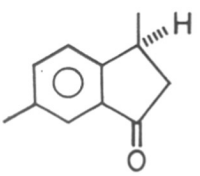


VI

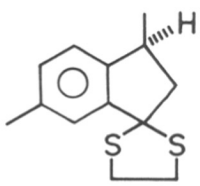


VII

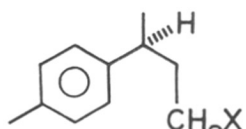
of five-membered ring in conjugation with benzene ring λ_{max} 242 mμ (ε = 10100) and 290 mμ (ε = 2368) comparable with that of indan-1-one which has λ_{max} 245 mμ (ε = 15900).[6] N.M.R. signals at 8.62τ (3H, doublet, J=7 c.p.s.) due to CH_3 attached to C-3, 7.61τ (3H, singlet) due to CH_3 attached to aromatic ring, 264 and 2.56τ (3H, protons attached to aromatic ring)] in high yields on treatment with polyphosphoric acid.[7] Condensation of (VII) with ethanedithiol in the presence of BF_3-ether complex[8,9] furnished the ethylenedithioderivative (VIII) [(absence of starting material shown by the IR spectrum - no band at 1720 cm^{-1} and UV spectrum (no band at 242 mμ); N.M.R. signals at 7.63τ (3H, singlet; CH_3 attached to aromatic ring), 6.59 and 6.53τ (4H; $\begin{matrix}CH_2\text{-}S\text{-}\\ CH_2\text{-}S\text{-}\end{matrix}$)]. It is interesting to note that though the indane (VIII) has the 'S' configuration at the only asymmetric centre it is strongly laevorotatory M_D = -152° in contrast to those of the type (II), which are dextro-



(VII)



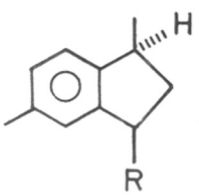
(VIII)



(II)

rotatory. 1,5-Dimethylindane (IX).* [N.M.R. signals at 8.76τ(3H, doublet; J=7 c.p.s.) due to C-1 methyl, 7.70τ (3H, singlet) due to C-5 methyl and 3.08τ(3H, protons attached to aromatic ring)] was prepared by the desulphurisation of (VIII) with Raney nickel,[8] or more conveniently by the reduction of the indanone (VII) with LAH-$AlCl_3$.[11]

Reduction of the indanone (VII) with sodium borohydride[12,13] yielded the indanol (X) [(ν_{max} 3300 cm^{-1}) due to OH group; N.M.R. signals at 8.72τ (doublet; J=7 c.p.s.) due to C-3 methyl group, 7.67τ (singlet) due to C-6 methyl group, 5.03 due to CH-OH)]. The OH group is expected to have the



(VII): R = O

(VIII): R = 

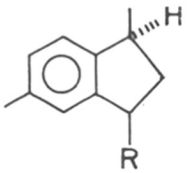
(IX): R = H_2

(X): R = OH

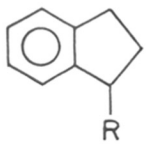
---

* When our investigation was in progress Brewster and Buta[10] prepared by a different approach a number of 1-substituted indanes. They have made the interesting observation that the dispersion curves of the indans are essentially enantiomeric to those of the corresponding α-phenylethyl compounds of the same absolute configuration. Their results indicate that conformational mobility has a significant effect on the optical rotation properties of aromatic compounds.

β-configuration in the indanol (X) from the method employed for its preparation; the hydride attack on the carbonyl group of indanone (VII) from the β-side is unlikely due to steric interference from the β-oriented methyl group at C-3. The assignment of R-configuration to C-1 hydroxyl in (X) is further supported by the positive shift in molecular rotation (ΔM_D = 129) on acetylation.*[10] The indanyl acetate (XIV) has two asymmetric centres and hence its O.R.D. curve may be expected to depend on the contributions of the asymmetric centres at C-1 and C-3; the contribution of the centre at C-1 is small since both 1-methylindane (XII)+ and 1,5-dimethylindane (IX) exhibit low rotation in the region 250-600 mμ. On the other hand 1-indanyl acetate (XIII)[10] exhibits comparatively strong rotation in the region 250-600 mμ. Hence the O.R.D. curve of indanylacetate (XIV) having



VII ; R = O; XIV ; R = OAc
IX ; R = H_2
X ; R = OH



XI ; R = OH
XII ; R = Me
XIII; R = OAc

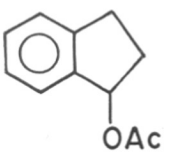
---

* (R)-(-)-1-indanol(XI) also shows a positive shift in molecular rotation on acetylation.

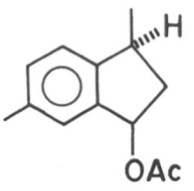
+ For ex. $(M)_{263}$ is -103 for 1-methylindane(XII);
$(M)_{266}$ is + 1730 for 1-indanyl acetate(XIII).[10]

the R-configuration at C-1 is expected to be comparable with the O.R.D. curve of indanylacetate (XIII). The O.R.D. curve of the indanylacetate (XIV) has been kindly determined by Professor Klyne and is comparable with the published O.R.D. curve of the acetate (XIII).[10]

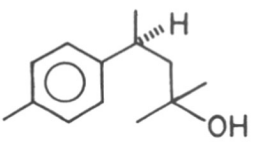
The tertiary alcohol (XVI) [(ν_{max} 3470 cm^{-1} due to -OH; N.M.R. signals at 7.68τ (3H, singlet) due to CH_3 attached to aromatic ring and 2.92τ (4H, aromatic protons)] prepared by the action of methyl magnesium iodide on ar-curcumone (XVII) furnished the laevorotatory indane (XVIII) on cyclialkylation in the presence of 90% sulphuric acid.[14,15] Dihydro-ar-turmerone (XIX) furnished the secondary alcohol (XX) (ν_{max} 3300 cm^{-1}) on reduction with lithium-aluminium hydride.



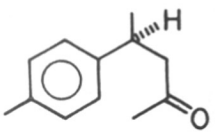
XIII



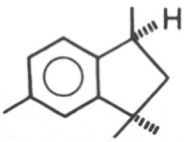
XIV



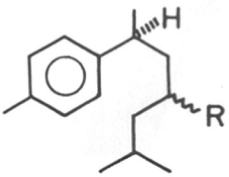
XVI



XVII



XVIII

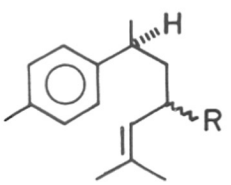


XXI ; R = O

XX ; R = OH

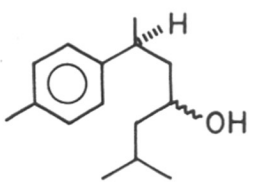
An attempt to prepare the indane (XXII) by cyclodehydration of the alcohol (XX) with 95% sulphuric acid[14,15] at room temperature was not successful; the starting material was recovered after the acid treatment.

The allylic tertiary alcohol (XXIV) and the allylic secondary alcohol (XXV) may be expected to yield readily the same resonance stabilised allylic carbonium ion (XXVI). The carbonium ion (XXVI) can cyclise to furnish either (XXVII) or (XXVIII) or a mixture of (XXVII) and (XXVIII). The alcohol (XXIV) was prepared by reducing ar-turmerone-oxide[16] (XXIII) with hydrazine.[17] The alcohol (XXV) (υ_{max} 3400 cm^{-1}) was prepared by reducing ar-turmerone (III) with sodium borohydride.[12,13] The alcohol (XXIV) on treatment with 80% sulphuric acid[14,15] furnished a product which was a mixture of two components since on gas-liquid chromatographic analysis, it exhibited two peaks with retention times of 3'41" and 6'48".* The same

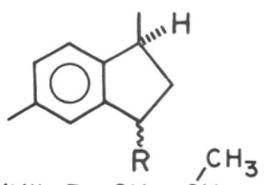


III; R = O

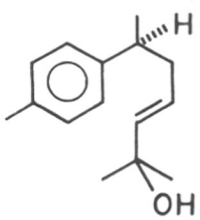
XXV; R = OH



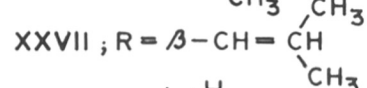
XX



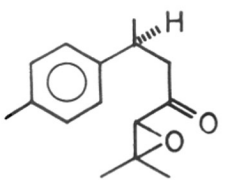
XXII; R = $CH_2-CH(CH_3)_2$



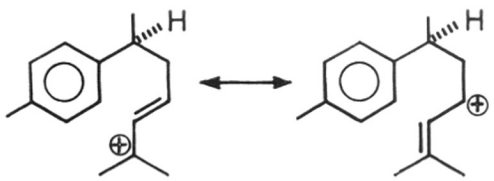
XXIV



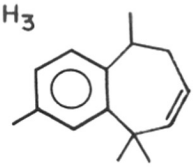
XXVII; R = β-CH=CH(CH$_3$)$_2$



XXIII



XXVI

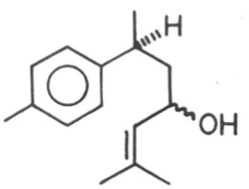


XXVIII

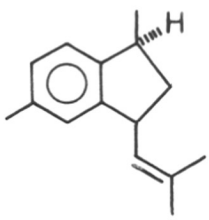
* Conditions are given in Experimental part.

product (as judged by G.L.C. behaviour) was also obtained when the alcohol (XXV) was treated with 90% sulphuric acid.[14,15] However, the N.M.R. spectrum of the product did not show signals in the vinyl proton region and hence does not contain either of the expected products (XXVII) and (XXVIII).

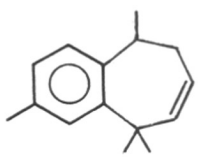
The N.M.R. spectrum of the benzylidene derivative (XXXI)[18] (doublet (J=16 c.p.s.) at 3.45τ due to C-2 vinyl proton) shows that the two vinyl protons are <u>trans</u> as indicated in the structure (XXXI). The ketone (XXXI) was cyclised at 110° in the presence of polyphosphoric acid[19] to furnish the suberanone (XXXII) (ν_{max} 1705 cm^{-1}; one proton signal in the region 5.2 to 5.8τ due to hydrogen attached to C-5). The Huang-Minlon[20] reduction of (XXXII) resulted in the hydrocarbon (XXXIV).



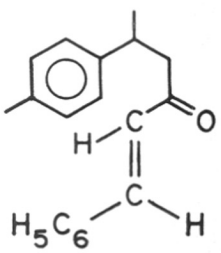
XXV



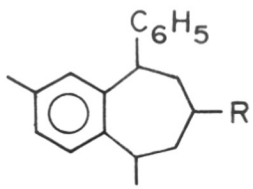
XXVII



XXVIII



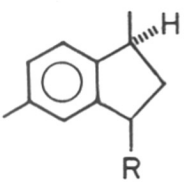
XXXI



XXXII ; R = O

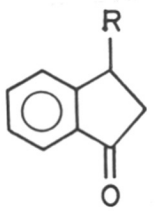
XXXIV; R = H_2

The (±) keto-ester (XXXVIII), prepared according to the literature method,[32] yielded a complex mixture on sodium borohydride reduction[12,13] and it was not possible to isolate any of the components in a pure state. The action of methyl magnesium iodide on (±) keto-ester (XXXVIII) also furnished a complex mixture.* On sodium borohydride reduction the (±) indanone (XXXIX) furnished the crystalline indanol (XLI) [υ_{max} 3230 cm^{-1}; N.M.R. signals at 8.72 τ (doublet; J=7 c.p.s.) due to CH_3 at C-3, 7.67 τ (singlet) due to CH_3 attached to aromatic ring and 5.03 τ due to hydrogen attached to C-1)]. The stereochemistry assigned at C-1 is on the basis of analogy with the course of reduction of (VII) and is further supported by the comparison of the N.M.R. spectra of the alcohols (X) and (XLI).



VII ; R = O

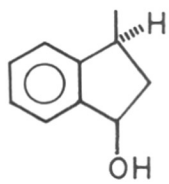
X ; R = OH



XXXVII ; R = COOH

XXXVIII ; R = COOEt

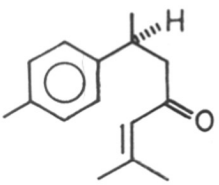
XXXIX ; R = CH_3



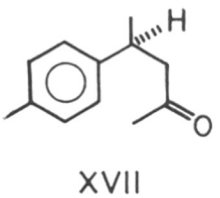
XLI

* The aim of the investigations was to prepare some optically active disubstituted indanes with the -OH group as one of the substituents. If encouraging results had been obtained in the (±) series, we would have extended the work to the (+) series. (+) Acid (XXXVII) is reported in literature.[30]

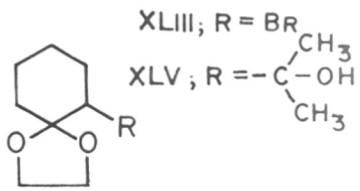
A number of synthesis of ar-turmerone[21,22] (III) as well as its degradation products[5,21] have been recorded in literature. However, we consider that it may be worthwhile to explore other approaches to the synthesis of ar-turmerone (III) and related products. We anticipated that the Grignard reagent prepared from bromoketal (XLIII)[23] would furnish the tertiary alcohol on treatment with acetone; the alcohol (XLV) on treatment with acid would yield the conjugated ketone (XLVI) as a result of deketalisation and dehydration.* The bromoketal (XLIII)[23] was

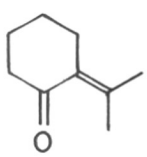


III

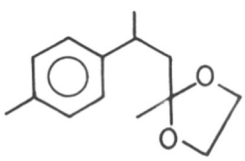


XVII

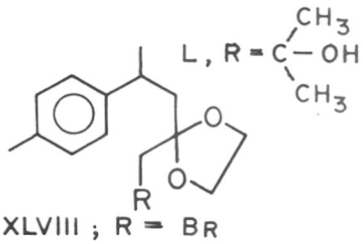




XLVI



XLVII



XLVIII ; R = BR

XLIX ; R = μg BR

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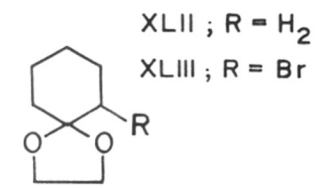
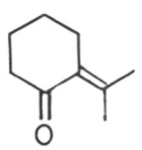
* Similarly it may be possible to convert ar-curcumone (XVII) to ar-turmerone (III) using the sequence (XVII) → (XLVII) → (XLVIII) → (XLIX) → (L) → (III). However, since this approach was not successful in the synthesis of 2-isopropylidene-cyclohexanone (XLVI), no attempt was made to synthesise ar-turmerone employing the above mentioned sequence.

prepared by the action of phenyltrimethylammonium-tribromide[24] on the ketal (XLII).[25] The bromo-compound was purified by fractionation through a spinning band column. The sample used for further investigation was pure as shown by its G.L.C. behaviour (single peak), the elemental analysis and N.M.R. spectrum. However, even after careful purification the bromoketal (XLIII) failed to react with magnesium, and we had to abandon the above synthetic approach to the 2-isopropylidene cyclohexanone (XLVI).

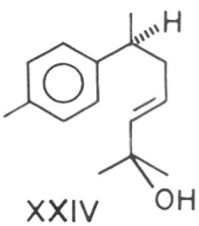
The tertiary alcohol (XXIV)[16] on chromic acid oxidation[26] furnished ar-turmerone (III). Similar types of rearrangements during oxidation of tertiary allylic alcohols are reported in literature.[26]

Dihydro-ar-turmerone (XIX) was brominated with molar proportion of bromine in acetic acid solution in the presence of hydrobromic acid. The resulting material, probably a mixture of bromo-compounds (LI) and (LII) was

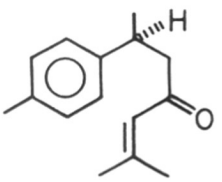




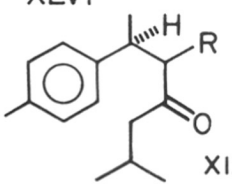
XLVI



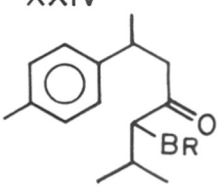
XXIV



III

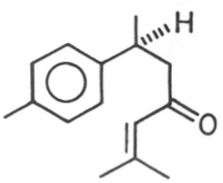


XIX , R = H2
LI , R = Br

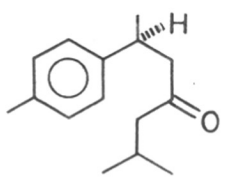


LII

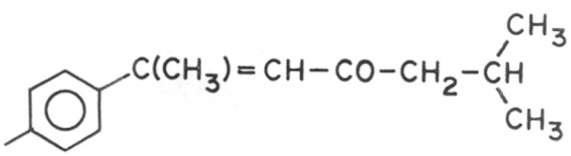
dehydrobrominated by refluxing with collidine[27] to furnish a product which on G.L.C. analysis showed three peaks with retention times of 4'36", 7'1" and 8'29".* The retention time of the first peak corresponds with that of dihydro-ar-turmerone (XIX) and the retention time of the second peak corresponds with that of ar-turmerone (III). The third peak is probably due to the ketone (LIV). The percentage of the three ketones (XIX), (III) and (LIV) has been estimated to be 10%, 54% and 36% by measurement of the areas of the peaks. The U.V. spectrum of the dehydrobromination product showed maxima at 230 mμ (ε = 8640) due to ar-turmerone and 281 mμ (ε = 6156), probably due to the isomeric ketone (LIV). On the basis of U.V. spectrum,+



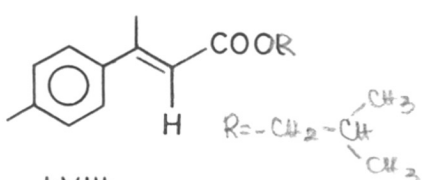
III



XIX



LIV



~~LVIII~~ LIX

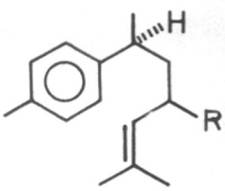
---

* Conditions are given in Experimental part.

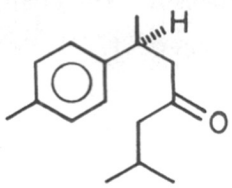
\+ Assuming that ε value for pure ketone (LIV) is 14761; ε value for the ester (LIX) is 14761.

the percentage of the ketone (LIV) in the dehydrobromination product has been estimated to be 38%. The presence of ar-turmerone in the dehydrobromination product was established by converting it to the 2,4-dinitrophenyl-hydrazone of ar-turmerone (LIII)[21] (identified by I.R. spectrum).

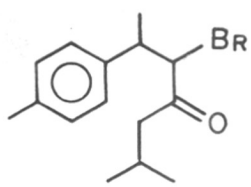
It is of interest to note that ar-turmerone (III) is formed to a larger extent than the isomeric ketone (LIV), on the bromination of dihydro-ar-turmerone and subsequent dehydrobromination. This result would suggest that during bromination of (XIX) attack at C-5 is favoured over attack at C-3* The tentative conclusion can be drawn that



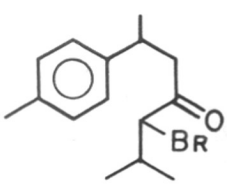
III , R = O
LIII , R = $NNHC_6H_3(NO_2)_2$



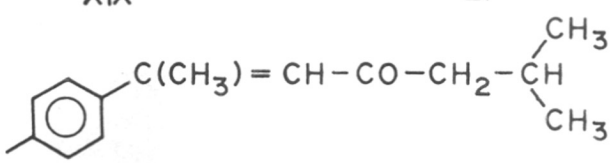
XIX



LI



LII

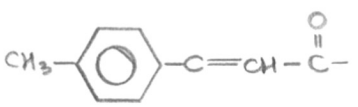


LIV

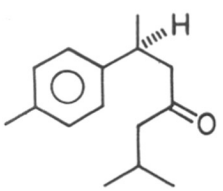
* It is assumed that the bromoketone (LII) furnishes ar-turmerone (III) and the bromoketone (LI) furnishes the ketone (LIV). Though this assumption is reasonable, the possibility of ar-turmerone being formed, at least to a limited extent, from the bromoketone (LI) cannot be excluded rigorously.

enolisation of dihydro-ar-turmerone (XIX) towards C-5 is more favourable than enolisation towards C-3.

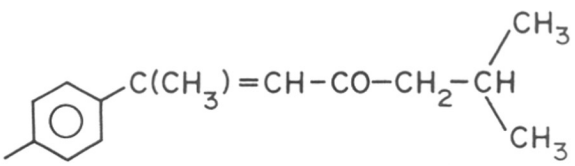
With a view to synthesise the ketone (LIV), β-p-tolylcrotonic acid (LVII)[28] was reacted with thionyl-chloride and the resulting product treated under controlled conditions with limited quantities of isobutylmagnesium-bromide. The resulting material was not the required ketone (LIV) as it analysed for $C_{15}H_{20}O_2$ and not for $C_{15}H_{20}O_1$. The U.V. spectrum (λ_{max} 272 mμ, ε = 14761) suggests the presence of the grouping



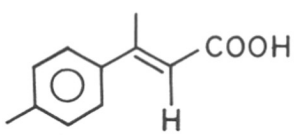
The presence of two oxygen atoms in the molecule of the product, the U.V. spectrum, the nature of reactants



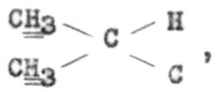
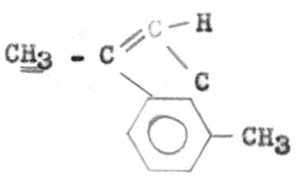
(XIX)



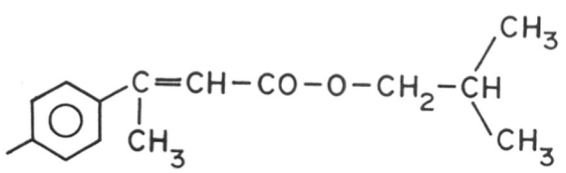
(LIV)



(LVII)

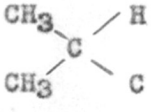
involved and the I.R. spectrum (ν_{max} 1715 and 1625 cm^{-1}) indicate that the product is the conjugated ester (LIX). This conclusion is supported by the N.M.R. spectrum, which showed two proton signals at 6.06 and 6.16 τ due to -O-CH_2-CH [other characteristic signals in the NMR at 9.03 τ (6H, doublet J=7 c.p.s.) due to  , 7.62 τ (3H, singlet) due to CH_3 attached to aromatic ring, 7.44 τ due to 

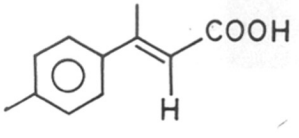
3.90 τ (1H, vinyl proton) and 2.96, 2.81, 2.69 and 2.55 τ (4H, due to aromatic protons)]. Further support for



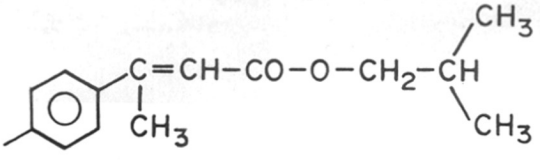
(LIX)

formulating the product as (LIX) was provided by isolating β-p-tolylcrotonic acid (LVII) (identified through m.p., mixed m.p. and I.R. spectrum) after its saponification with alkali.

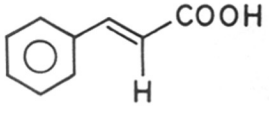
The interesting results obtained in the Grignard reaction mentioned above prompted us to extend the study to the cinnamic acid (LX). Cinnamic acid (LX) was treated with thionyl chloride and the resulting material treated with isobutylmagnesium bromide as in the previous case. The product has been identified as the isobutylester (LXII) on the basis of elemental analysis, I.R. spectrum (ν_{max} 1710 and 1630 cm^{-1}), U.V. spectrum (λ_{max} 272 mμ; ε = 24620), and N.M.R. spectrum [(signals at 9.02 τ (6H, doublet, J=7 c.p.s., ), 6.08 τ (2H, doublet; J=7 c.p.s.



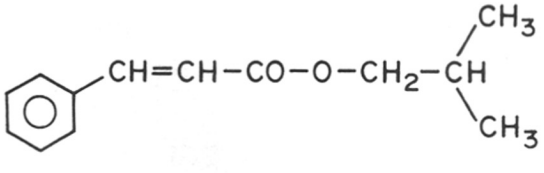
(LVII)



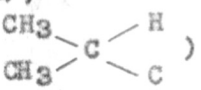
(LIX)

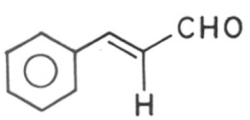


(LX)

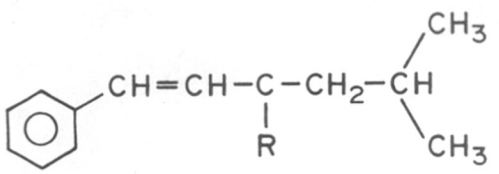


(LXII)

-OCH$_2$ - CH ), 3.68 τ (1H, doublet; J=17 c.p.s., H attached to C-2), and at 2.42 τ (doublet; J=17 c.p.s., H attached to C-1)]. Reaction of cinnamaldehyde (LXIII) with isobutyl magnesium bromide furnished the allylic alcohol (LXIV) which was oxidised to the ketone (LXV) [ν_{max} 1675 and 1600 cm^{-1}; λ_{max} 278.5 mμ (ε = 22274); N.M.R. signals at 9.07 τ (6H, doublet; J=7 c.p.s., ) and 3.41 τ (1H, doublet, J=17 c.p.s., H attached to C-5)].



(LXIII)



(LXIV): R=OH

(LXV): R=O

EXPERIMENTAL

(+) Ar-turmerone (III)

Turmerone (V) (10 g., obtained by fractionation of commercial turmeric oil) in acetone (140 ml) was oxidised with the Jones reagent (34 ml). The Jones reagent was added in portions to the cold reaction mixture and the reaction was completed by keeping the reaction mixture at the room temperature for 2 hrs. After dilution with water, most of the acetone was removed by distillation in vacuo (temperature of the bath did not exceed 60°) and the residue was extracted with ether. Ether extract was washed with cold sodium carbonate solution and water, dried and ether was removed. Distillation of the residue furnished (+) ar-turmerone (3.2 g), b.p. 170°(bath)/9 mm., which was identified by its specific rotation and refractive index.[21]

G.L.C. On using the polyester column maintained at 220° (flow rate of hydrogen 0.8 ml/sec), ar-turmerone obtained by Jones oxidation of turmerone (V) gave single peak, retention time 7'1". Under same conditions, the authentic sample of ar-turmerone had the identical retention time (7'1").

3,6-Dimethylindan-1-one (VII)

Polyphosphoric acid was prepared by adding phosphoric acid (13.5 ml) in one lot to P_2O_5 (22.5 g) and heating the mixture for 1 hr. at 100° under anhydrous conditions.

To polyphosphoric acid, prepared as above, 3-p-tolylbutanoic acid (VI) (3.019 g) prepared by ozonolysis of ar-turmerone (III), was added, the reaction mixture was well stirred with the glass rod, heating was continued for another 1 3/4 hr, then it was cooled, poured into the crushed ice and extracted with ether. Ether extract was washed with sodium carbonate solution and water, dried and ether was removed. Distillation of the residue furnished dimethylindanone (VII), b.p. 150°(bath)/6 mm. (1.5904 g). The starting acid (1.0114 g) was recovered from sodium carbonate washings.

Specific rotation: $(\alpha)_D$ + 13° (c, 5.28% in chloroform).

Analysis: Found: C, 82.66; H, 7.59. $C_{11}H_{12}O$ requires: C, 82.46; H, 7.55%.

I.R. spectrum (liq. film; p.150) shows prominent bands at: 2950, 1720, 1620, 1575, 1480, 1450, 1420, 1400, 1370, 1320, 1275, 1245, 1160, 1120, 1050 and 825 cm^{-1}.

U.V. spectrum (in ethanol): λ_{max} 242.5 mμ (ε = 10166) and λ_{max} 290 mμ (ε = 2368).

G.L.C. It showed a single peak, retention time 5'54" (polyester column maintained at 200°, the flow rate of hydrogen 0.9 ml/sec).

N.M.R. spectrum (p.169) is discussed in the theoretical part in this chapter.

1-Ethylenedithio-3,6-dimethylindan (VIII)

BF_3-ether complex (2.7 ml) and ethanedithiol (2.7 ml) were added to a solution of the ketone (VII) (1 g) in glacial acetic acid (32 ml) and the reaction was allowed to proceed at room temperature overnight. The solution was then diluted with water and extracted with ether. Ether extract was washed with water, 10% sodium carbonate solution and again with water and dried. Removal of the solvent and distillation of the residue furnished the thioketal (VIII) (0.8930 g), b.p. 195° (bath)/3 mm., as a thick oil.

Specific rotation: $(\alpha)_D$ - 64° (c, 5.07% in chloroform)

Analysis: Found: C, 67.14; H, 7.36; S, 28.23% (the end point for S estimation was not quite satisfactory during the estimation of S). $C_{13}H_{16}S_2$ requires: C, 66.06; H, 6.79; S, 27.15%.

I.R. spectrum (liquid film; p.151) shows prominent bands at: 2950, 2560, 1620, 1480, 1430, 1270, 1220, 1145, 962 and 820 cm^{-1}.

U.V. spectrum (in ethanol) λ_{max} 242.5 mμ (ε = 585). This may be due to the presence of 5% of unreacted indanone.

N.M.R. spectrum (p.169) shows signals at 8.69τ (3H, doublet J=7 c.p.s., CH_3 attached to C-3), 7.63τ(3H, singlet, CH_3 attached to aromatic ring), 6.59 and 6.53τ (4H, CH_2-S-, CH_2-S-), 3.02 and 2.72τ (3H, aromatic protons).

1,5-Dimethylindan (IX)[33]

(a) By reduction of ketone (VII) with LAH-AlCl3

Lithium aluminium hydride (1.4210 g., 40% excess) was added to a suspension of anhy. $AlCl_3$ (3.1179 g) in dry ether (20 ml). After the vigorous reaction has subsided, the ketone (1.0736 g) in dry ether (15 ml) was added dropwise during 20 minutes, followed by heating under reflux for 3 hrs with stirring. The reaction mixture was decomposed at 0° by addition of 1:1 mixture of acetone and ether (10 ml), water (60 ml) and 10% HCl (35 ml) and then extracted with ether. Ether extract was washed with cold sodium bicarbonate solution and water, dried and ether was removed. Residue was chromatographed over alumina, gr.I (100 g) and eluted with pet.ether 40-60°. Removal of the solvent furnished mainly the hydrocarbon (containing 5% of starting ketone, which was identified by G.L.C.) $(\alpha)_D$ - 1.5° (c, 8.67% in chloroform), which was distilled over sodium to give pure hydrocarbon (IX) (0.8400 g), b.p. 118°(bath)/13 mm.

Specific rotation: $(\alpha)_D$ - 4° (c, 9.06% in chloroform).

Analysis : Found: C, 90.07; H, 9.72. $C_{11}H_{14}$ requires:
C, 90.35; H, 9.65%.

I.R. spectrum (liquid film; p.152) shows bands at: 2935, 1620, 1480, 1450, 1370, 1310, 1200, 1140, 1075, 1040, 950, 876 and 810 cm^{-1}.

G.L.C. It gave a single peak, retention time 2'20". Under same conditions (polyester column maintained at 180°, flow rate of hydrogen 0.95 ml/sec), the starting ketone (VII) gave a single peak, retention time 17'26".

N.M.R. spectrum (p.170) is discussed in the theoretical part of this chapter.

(b) By desulphurisation of thioketal (VIII)

Thioketal (VIII) (0.8930 g) was stirred under reflux with absolute alcohol (50 ml) and Raney nickel catalyst (5.74 g., moist with ethanol) for 21 hrs, catalyst was filtered off and washed with small amount of ethanol. Filtrate, after removal of the solvent and distillation furnished dimethylindan (IX) (0.3925 g), b.p. 100°(bath)/2 mm., which was purified by distillation over sodium.

Analysis. Found: C, 89.20; H, 9.37. $C_{11}H_{14}$ requires:
C, 90.35; H, 9.65%.

I.R. spectrum (liquid film) shows prominent bands at: 2950, 1620, 1490, 1450, 1380, 1350, 1315, 1130, 1040, 1010, 950, 870, 820 and 760 cm^{-1}.

G.L.C. The product of desulphurisation was compared in GLC [180° (polyester column, flow rate of hydrogen 0.9 ml/sec)] with the ketone (VII). It gave two peaks with retention times of 2'18" and 4'20". Under identical conditions the retention time for ketone (VII) was 17'26" and for the dimethylindan (IX) prepared by method 'a' was 2'20". This shows that method 'b' gives dimethylindan (IX) contaminated with another compound (which has not been identified so far) having retention time of 4'20".

3β,6-dimethylindan-1β-ol (X)

Ketone (VII) (0.8271 g) and sodium borohydride (0.2904 g) were dissolved in ethanol (100 ml) and the reaction mixture was kept overnight at the room temperature. The excess of the reagent was destroyed by addition of a small amount of acetic acid, reaction mixture was diluted with water, most of ethanol was removed (vacuum distillation) and the residue was kept in cold. White solid which crystallised out was filtered and recrystallised from dilute ethanol to give alcohol (X) (0.3908 g), m.p. 67-69°. After sublimation under vacuum this alcohol had m.p. 69-70°. From the filtrate and mother liquor a second crop (0.23 g) of the alcohol (X) was isolated.

Specific rotation: $(\alpha)_D$ - 5° (c, 10.86% in chloroform).
Analysis: Found: C, 81.49; H, 9.81. $C_{11}H_{14}O_1$ requires:
C, 81.44; H, 8.70%.

I.R. spectrum (in Nujol; p.153) shows prominent bands at: 3300, 2900, 1460, 1370, 1330, 1310, 1280, 1140, 1090, 1055, 975, 890, 878 and 815 cm^{-1}.

G.L.C. Alcohol (X) gave a single peak, retention time 5'12". Under same conditions (polyester column maintained at 220°, flow rate of hydrogen 0.95 ml/sec.) the starting ketone (VII) had retention time 4'10".

N.M.R. spectrum (p.170) showed signals at: 8.72τ (3H, doublet J=7 c.p.s., CH_3 attached to C-3), 7.67τ (3H, singlet, CH_3 attached to aromatic ring), 3.00 and 2.91τ (3H, protons attached to aromatic ring) and 5.03τ (1H, multiplet, H attached to C-1).

3β,6-Dimethyl-1β-acetoxyindan (XIV)

Alcohol (X) (0.3185 g) was heated on the steam bath with dry pyridine (0.5 ml) and acetic anhydride (0.5 ml) for 2 hrs, solvents were removed by distillation under vacuum (water aspirator), residue diluted with water and extracted with ether. Ether extract, after washing with water, drying and removal of the solvent, furnished the acetate (XIV) (0.3537 g) which was distilled to give 0.1932 g, b.p. 110° (bath)/0.2 mm.

Specific rotation: $(\alpha)_D$ + 60° (c, 12.78% in chloroform)

Analysis: Found: C, 76.49; H, 8.20. $C_{13}H_{16}O_2$ requires: C, 76.44; H, 7.90%.

I.R. spectrum (liquid film; p.154) shows prominent bands at: 2950, 1760, 1495, 1450, 1370, 1235, 1145, 1100, 1040, 972, 910 and 820 cm^{-1}.

N.M.R. spectrum (p.171) shows signals at: 8.47τ (3H, doublet, J=7 c.p.s., CH_3 attached to C-3), 7.98τ (3H, singlet CH_3-CO-O-), 7.66τ(3H, singlet, CH_3 attached to aromatic ring) and 3.96τ (1H, multiplet, H attached to C-1).

3β,6-dimethyl-1β-benzoyloxyindane (XV)

Benzoylchloride (0.18 ml) was added to the ice-cold solution of alcohol (X) (0.1651 g) in dry pyridine (0.6 ml). Reaction mixture was allowed to stand at the room temperature for 24 hrs, diluted with water and extracted with ether. Ether extract was washed with sodium carbonate solution and water, dried and ether was removed. Residue (0.1805 g) was distilled in vacuo to give the benzoate (XV) (0.1492 g), b.p. 160°(bath)/ 0.6 mm.

Specific rotation: $(\alpha)_D$ - 21° (c, 11% in chloroform)

Analysis: Found: C, 81.00; H, 6.78. $C_{18}H_{18}O_2$ requires C, 81.17; H, 6.81%.

I.R. spectrum (liquid film; p.155) shows prominent bands at: 2950, 1720, 1600, 1490, 1450, 1310, 1265, 1175, 1115, 1070, 1030, 820 and 712 cm^{-1}.

2-Methyl-4-p-tolylpentane-2-ol (XVI)

To an ice cooled solution of methyl magnesium iodide (from 4.5 ml of methyl iodide and0.9 g. of Mg) in dry ether (20 ml), ar-curcumone (XVII) (2.1810 g) in dry ether (7 ml) was added dropwise. The mixture was heated under reflux for 10 minutes (with stirring), then cooled in ice and decomposed by pouring it into crushed ice (70 g) containing conc. sulphuric acid (2.4 ml). Reaction product was extracted with ether and ether extract was washed with 10% sulphuric acid and water. After drying, the solvent was removed and the residue distilled in vacuo to give the tertiary alcohol (XVI) (1.625 g), b.p. 115°(bath)/3.75 mm.

Refractive index: n_D^{26} 1.5009.

Specific rotation: $(\alpha)_D$ + 14° (c, 10.09% in chloroform).

Analysis : Found: C, 80.97; H, 10.97. $C_{13}H_{20}O$ requires: C, 81.20; H, 10.48%.

I.R. spectrum (liquid film) p.156 shows prominent bands at: 3470, 3000, 1520, 1470, 1380, 1210, 1140, 1115, 1020, 935, 897 and 820 cm^{-1}.

G.L.C. In GLC tertiary alcohol (XVI) gave a single peak, retention time 2'54" (polyester column maintained at 220°, flow rate of hydrogen 0.95 ml/sec).

N.M.R. spectrum (p.172) is discussed in the theoretical part of this chapter.

1,1,3,6-Tetramethylindan (XVIII)

Tertiary alcohol (XVI) (0.9781 g) was added dropwise to the cold, stirred (90%) sulphuric acid (1.5 ml) and stirring was continued for 2 1/2 hrs. The reaction mixture was diluted with water and extracted with ether. Ether extract was washed with sodium carbonate solution and water, dried and ether was removed. The residue (0.7812 g) (no band for -OH in the I.R. spectrum) was distilled over sodium to give the hydrocarbon (XVIII) (0.4522 g), b.p. 110°(bath)/10 mm.

Specific rotation: $(\alpha)_D$ - 6.8° (c, 9.44% in chloroform)

Analysis: Found C, 88.76; H, 10.62. $C_{13}H_{18}$ requires: C, 89.59; H, 10.41%.

I.R. spectrum (liquid film; p.157) shows prominent bands at: 2950, 1620, 1490, 1450, 1370, 1360, 1310, 1160, 1085, 1040, 883 and 815 cm^{-1}.

G.L.C. It gave a single peak, retention time 2'2" under following conditions: polyester column, flow rate of hydrogen 1.05 ml/sec., temperature 166°.

2-Methyl-6-p-tolylheptane-4-ol (XX)

A solution of dihydro-ar-turmerone (XIX) (3.5 g) (obtained by hydrogenation of ar-turmerone), in dry ether (15 ml) was slowly added to a suspension of LAH (2.5 g) in dry ether (25 ml), kept cooled at 0°. The reaction mixture

was then heated under reflux for 12 hrs, cooled to 0° and the excess of LAH was decomposed by addition of water, and 10% HCl. Extraction with ether, washing of the ether extract with water, drying and removal of the solvent furnished a residue which was distilled to give the alcohol (XX) (?.98 g), b.p. 125-135°(bath)/0.4 mm.

Specific rotation: $(\alpha)_D$ + 20° (in chloroform)

Analysis: Found: C, 82.08; H, 11.40. $C_{15}H_{24}O_1$ requires: C, 81.76; H, 10.98%.

I.R. spectrum (liquid film; p.158) shows prominent bands at: 3300, 2900, 1505, 1450, 1362, 1215, 1167, 1138, 1011, 950, 918, 835 (815) and 727 cm^{-1}.

3-Methyl-4-methoxy-6-p-tolylheptane (XXI)

A mixture of the alcohol (XX) (1.0 g), dry benzene (50 ml) and potassium metal (0.6 g) was refluxed for 1 hr with occasional shaking. Methyl iodide (20 ml) was added to the reaction mixture, and it was refluxed for another 3 hrs. After keeping the reaction mixture at room temperature overnight, the excess of potassium metal was destroyed by slow addition of methanol (15 ml) and the solvent was removed leaving the white residue, which was extracted with pet.ether 40-60°. Removal of the solvent and distillation of the residue furnished the methylated product (XXI), b.p. 130-140°(bath)/ 1.4 mm.

Specific rotation: $(\alpha)_D$ + 22°.

Analysis. Found: C, 82.10; H, 11.63. $C_{16}H_{26}O$ requires: C, 81.99; H, 11.18%.

I.R. spectrum (liquid film; p.159) shows prominent bands at: 2900, 1505, 1450, 1367, 1143, 1092, 1020, 815 and 723 cm^{-1}.

Cyclodehydration of 6-p-tolyl-2-methylhept-3-ene-2-ol(XXIV)

6-p-Tolyl-2-methylhept-3-ene-2-ol (XXIV) was prepared from epoxy-ar-turmerone (XXIII) by the method described in the literature.[16] Epoxy-ar-turmerone (XXIII)[16] was obtained by treating ar-turmerone with 30% hydrogen peroxide in the presence of NaOH solution; its properties (n_D^{24} 1.5010 and IR spectrum) are in good agreement with the reported values.[16] The epoxide (XXIII) was reduced with 80% N_2H_4 to give the tertiary alcohol (XXIV)[16] ($n_D^{24.5}$ 1.5075, I.R. bands at: 3400, 3000 1900, 1650, 1520, 1450, 1385, 1160, 1040, 1020, 975, 918, 820, and 725 cm^{-1}), in agreement with data quoted in literature.[16]

Alcohol (XXIV) (1.5 g) was added dropwise to the ice cooled, stirred 89% sulphuric acid (3 ml). Stirring was continued for another 2 hrs at room temperature, then reaction mixture was diluted with water and extracted with ether. The ether extract was washed with cold sodium carbonate solution and with water, then it was dried and ether was removed.

The residue (1.0035 g) (no band for OH in the I.R. spectrum), was chromatotographed over alumina, gr.I (30 g) and eluted with pet.ether 40-60° (200 ml). Removal of the solvent and distillation of the residue over sodium and under reduced pressure furnished the reaction product, b.p. 128° (bath)/ 9 mm.

Analysis: Found: C, 88.65; H, 10.74. $C_{15}H_{20}$ requires: C, 89.94; H, 10.06%.

I.R. spectrum (liquid film) shows prominent bands at: 2950, 1620, 1510, 1450, 1375, 1125, 815 and 725 cm^{-1}.

G.L.C. It gave two peaks, retention times: 3'41" and 6'50" (polyester column maintained at 158°, flow rate of hydrogen 0.9 ml/sec.).

Chromic acid oxidation of 6-p-tolyl-2-methylhept-3-ene-2-ol (XXIV)

Alcohol (XXIV) (0.1014 g), water (0.8 ml), acetic acid (0.1 ml) and benzene (0.2 ml) were well stirred and 50% sulphuric acid (0.3 ml) was added in one lot and with stirring. Then solution of sodium dichromate (0.2056 g) in water (0.4 ml) was added dropwise, while the reaction mixture was stirred and cooled in the water. Temperature of the bath was raised till 50-60° and maintained for 1 1/2 hrs, then the reaction mixture was diluted with water and extracted with ether. Ether extract was washed with water,

dried and ether was removed to give ar-turmerone (III) (0.0600 g), which was distilled in vacuo, b.p. 160° (bath)/ 8 mm.

I.R. spectrum (liquid film) is identical with that of an authentic sample of ar-turmerone (III).

G.L.C. Polyester column, maintained at 224° was used, flow rate of hydrogen was 0.7 ml/sec. Chromic acid oxidation product was compared in G.L.C. with the authentic ar-turmerone. Both have shown peaks with identical retention time (7'1").

2,4-Dinitrophenyl hydrazone.[21] The 2,4-dinitrophenyl hydrazone derivative prepared from the above oxidation product was purified through chromatography over alumina, gr.II and identified as (LIII) on the basis of its IR spectrum.

2-Methyl-6-p-tolylhept-2-en-4-ol (XXV)

Ar-turmerone (III) (3 g) and sodium borohydride (1.85 g) were dissolved in ethanol (300 ml), the reaction mixture was kept at the room temperature overnight and the excess of the reagent was destroyed by addition of small amount of acetic acid. The reaction mixture was diluted with water, most of ethanol was removed and the residue was extracted with ether. Ether extract was washed with water and dried. After removal of the solvent, the residue was distilled in vacuo to give the alcohol (XXV) (2.5138 g), b.p. 112° (bath)/0.2 mm.

Refractive index: n_D^{24} 1.5014.

Specific rotation: $(\alpha)_D$ + 10° (c, 10.71% in chloroform)

Analysis: Found: C, 82.17; H, 10.73. Calc. for $C_{15}H_{22}O$1: C, 82.51; H, 10.16%.

I.R. spectrum (liquid film; p.160) shows a prominent band for OH group at 3400 cm^{-1}. Other prominent bands at: 2950, 1620, 1450, 1380, 980, 820 and 725 cm^{-1}.

Cyclodehydration of 2-methyl-6-p-tolylhept-2-en-4-ol (XXV)

Alcohol (XXV) (2.2777 g) was added dropwise to the ice cooled, stirred 90% sulphuric acid (4.5 ml). Stirring was continued for another 2 hrs at room temperature, the reaction mixture was diluted with water and extracted with ether. The ether extract was washed with cold sodium carbonate solution and with water, then dried and ether removed. Residue (1.9456 g) did not show band for -OH in its I.R. spectrum. It was chromatographed over alumina, gr.I and eluted with pet.ether 40-60° (400 ml). Residue obtained after removal of solvent was distilled in vacuo over sodium, to give the reaction product, b.p. 125°(bath)/ 15 mm.

Analysis: Found: C, 88.35; H, 12.00. $C_{15}H_{20}$ requires: C, 89.94; H, 10.06%.

I.R. spectrum (liquid film) shows prominent bands at: 2950, 1620, 1520, 1450, 1375, 1125, 820 and 723 cm^{-1}.

G.L.C. The product of cyclodehydration of (XXV) shows two peaks, retention times: 3'41" and 6'48". Under identical conditions (polyester column, maintained at 158°, flow rate

of hydrogen 0.9 ml/sec), the product of cyclodehydration of (XXIV) shows two peaks, retention times: 3'41" and 6'50".

2,4-Dimethyl-6-p-tolylheptane-4-ol (XXIX)

To an ice cooled solution of methyl magnesium iodide (from 7.8 ml of methyl iodide and 1.2191 g. of magnesium) in dry ether (40 ml), dihydro-ar-turmerone (XIX) (3 g) (obtained by hydrogenation of ar-turmerone in the presence of 10% Pd-C catalyst) was added slowly and with stirring. The reaction mixture was refluxed for 15 minutes, cooled and poured into crushed ice (80 g) containing conc. sulphuric acid (2.5 ml). Reaction product was extracted with ether, washed with 10% sulphuric acid and with water, dried and ether was removed. Vacuum distillation of the residue furnished (XXIX), b.p. 150° (bath)/9 mm. (2.653 g).

Refractive index: n_D^{26} 1.4905

Specific rotation: $(\alpha)_D$ + 15° (c, 7.98% in chloroform).

Analysis: Found: C, 82.24; H, 11.68. $C_{16}H_{26}O_1$ requires: C, 81.90; H, 11.18%.

I.R. spectrum (liquid film) shows a prominent band at 3400 cm^{-1}, Other bands at: 2900, 1500, 1475, 1360, 1140, 1105, 1080, 1020, 943, 815 and 720 cm^{-1}.

G.L.C. It gave a single peak, retention time 2'10". Under identical conditions (polyester column maintained at 214°,

flow rate of hydrogen 0.6 ml/sec), dihydro-ar-turmerone (XIX) gave a single peak, retention time 2'1".

Cyclodehydration of 2,4-dimethyl-6-p-tolylheptane-4-ol (XXIX)

Alcohol (XXIX) (2 g) was added dropwise to the ice cooled and stirred 90% sulphuric acid (3 ml) and the stirring was continued for another 2 hrs at room temperature. Reaction mixture was diluted with cold water, extracted with ether, ether extract was washed with cold sodium carbonate solution and with water, dried and ether was removed. Residue (1.3754 g) did not show band for OH in its I.R. spectrum. It was distilled in vacuo over sodium to give (XXX) 1.0222 g., b.p. 150° (bath)/12 mm.

Specific rotation: $(\alpha)_D$ + 17° (c, 10.23% in chloroform)

Analysis: Found: C, 88.65; H, 11.60. $C_{16}H_{24}$ requires: C, 88.82; H, 11.18%.

I.R. spectrum (liquid film) shows prominent bands at: 3000, 1530, 1455, 1370, 1165, 1020, 885, 818 and 730 cm^{-1}.

G.L.C. It shows that the cyclisation product is a mixture of one major compound (retention time 4'50") and two minor components (retention times: 5'55" and 7'10"). Conditions: polyester column maintained at 166°, flow rate of hydrogen 1.05 ml/sec.).

1-Phenyl-5-p-tolylhex-1-en-3-one (XXXI)
(Benzylidene derivative of ar-curcumene)

Ar-curcumone (XVII) (3.0 g) and freshly distilled benzaldehyde (7.0 g) were dissolved in ethanol (35 ml) and 5N NaOH solution (1.7 ml) was added. The reaction mixture was shaken well and allowed to stand overnight at the room temperature. The solid which crystallised out was recrystallised from ethanol to give benzylidene derivative (XXXI) (2.3 g), m.p. 104°. Lit. value[18] m.p. 106°.

I.R. spectrum (in Nujol; p.161) shows prominent bands at: 2900, 1675, 1640, 1470, 1370, 1280, 1115, 980, 820, 758 and 722 cm^{-1}.

U.V. spectrum (in ethanol): λ_{max} 288 mμ (ε = 10626).

N.M.R. spectrum (p.175) shows signals at 8.57τ (3H, doublet, J=7 c.p.s., CH_3 on C-5), 7.72τ (3H, singlet, CH_3 attached to aromatic ring), 6.5 - 7.5τ (3H, hydrogens attached to C-4 and C-5), 3.45τ (1H, doublet J=16 c.p.s., H attached to C-2), 2.93τ (4H, singlet, protons attached to disubstituted benzene ring), 2.4 - 2.8τ (6H, protons attached to monosubstituted benzene ring and proton attached to C-1; the pattern of signals in this region is identical with the pattern of signals due to trans-4-phenyl-3-buten-2-one[31] (XXXV) in the same region).

2,5-Dimethyl-9-phenyl-7-oxo-benzosuberan (XXXII)

Benzylidene derivative of ar-curcumone (XXXI) (1.46 g), m.p. 104°, was cyclised by heating, in the presence of polyphosphoric acid (prepared from 12 g. of P_2O_5 and 7.3 ml of phosphoric acid) from an initial temperature of 80° to a final temperature of 110° during 30 minutes. After cooling, the reaction mixture was poured on crushed ice, and extracted with ether. Ether extract was washed with cold sodium carbonate solution and water and dried. Residue, obtained after removal of ether contained some unreacted conjugated ketone (proved by its I.R. spectrum and U.V. spectrum). It was dissolved in 50% ethanol (13.5 ml) containing KOH (1.3 g) and refluxed for 1 hr. After dilution with water, the reaction mixture was subjected to steam distillation during 2 hrs (to remove ar-curcumone and benzyldehyde), then cooled, acidified and extracted with ether. Ether extract was washed with water and dried. Removal of ether furnished benzosuberanone (XXXII) (1.0166 g), which was distilled in vacuo to give 0.90 g, b.p. 190°(bath)/0.4 mm. of pure ketone (XXXII) (U.V. spectrum does not show presence of conjugated ketone).

Specific rotation: $(\alpha)_D$ + 11.4° (c, 2.015% in chloroform).
Analysis: Found: C, 86.26; H, 7.98. $C_{19}H_{20}O_1$ requires: C, 86.32; H, 7.63%.

I.R. spectrum (in Nujol; p.162) shows prominent bands at: 2900, 1705, 1600, 1490, 1450, 1370, 1030, 818 and 698 cm^{-1}. N.M.R. spectrum (p.173) shows signals at: 8.70τ (3H, doublet, J=7 c.p.s., CH_3 attached to C-1), 7.70τ (3H, singlet, CH_3 attached to aromatic ring) and 5.2 - 5.8τ (1H, broad, H attached to C-5).

2,5-Dimethyl-9-benzosuberan (XXXIV)

Benzosuberanone semicarbazone (XXXIII) (0.70 g) (gummy material prepared from 0.7 g. ketone) was added to the solution of KOH (1.81 g) in freshly distilled diethylene-glycol (6.3 ml). The mixture was refluxed at 200-210° for 2 hrs in an atmosphere of nitrogen, diluted with water and extracted with ether. Ether extract was washed with water and dried. Removal of solvent furnished 0.5 g. of residue which was chromatographed over alumina, gr.I (15 g.). Pet. ether (60-80; 200 ml) eluted material was distilled in vacuo to give benzosuberan (XXXIV) (0.042 g), b.p. 170°(bath)/2 mm.

Analysis: Found: C, 91.49; H, 9.47. $C_{19}H_{22}$ requires: C, 91.22; H, 8.78%.

I.R. spectrum (trace of Nujol; p.163) shows prominent bands at: 2940, 1600, 1500, 1485, 1450, 1370, 1030, 970, 820, 747, 725 and 700 cm^{-1}.

N.M.R. spectrum (p. 173) shows signals in the region 5.5-6.0τ (1H, broad, H attached to C-1).

1-Oxo-indane-3-carboxylic acid (XXXVII)[30]

The starting material for preparation of this acid was phenylsuccinic acid (prominent I.R. bands at: 2900, 1700, 1470, 1370, 1320, 1245, 1200, 930, 729 and 700 cm^{-1}) which was prepared as described in the literature.[29] Phenylsuccinic acid (10 g) was heated at 100° with thionyl chloride (12.5 ml) for 45 minutes, then nitrobenzene (25 ml) and powdered anhydrous aluminium chloride (11 g) were added. The reaction mixture was kept at 80° for 1 1/2 hr, poured in water (250 ml) and nitrobenzene was removed by steam distillation. Remaining solution was treated with activated charcoal, filtered and cooled in ice. The solid which crystallised out was filtered off, washed with water and dried at the room temperature to give hydrated acid, m.p. 84°. The hydrated acid on heating at 100° under reduced pressure, melted and then solidified to anhydrous acid (XXXVII) (4.8 g), m.p. 120°. Lit. value[30] m.p. 120-7°.

I.R. spectrum (in Nujol) shows prominent bands at: 2940, 1725, 1690, 1600, 1470, 1375, 1190, 1050, 815, 770 and 725 cm^{-1}.

The ethyl ester of 1-oxo-indane-3-carboxylic acid (XXXVIII)[32] was prepared by azeotropic method. The product obtained was distilled at 165-180°(bath)/0.5 mm.
I.R. spectrum (in Nujol; p.164 shows a prominent band at 1725 cm^{-1}. Other prominent bands at: 2900, 1585, 1450, 1370, 1335, 1240, 1180, 1050 and 760 cm^{-1}.

N.M.R. spectrum (p.172) shows signals at: 8.70τ (3H, triplet, J=7 c.p.s., -O-CH_2-CH_3), 7.22, 7.09, 7.00τ(2H, protons attached to C-2), 5.95, 5.90, 5.84, 5.71, 5.60τ (3H, H attached to C-3 and -O-CH_2-CH_3) and 2.15 - 2.80τ (4H, protons attached to aromatic ring).

(±) 3-Methylindan-1-one (XXXIX)[34]

(±) 3-Phenylbutanoic acid (XL) (3.4 g) was heated for 2 hrs at 100° with polyphosphoric acid (prepared from 15.3 ml of phosphoric acid and 25.72 g. of P_2O_5). under anhydrous conditions. The reaction mixture was poured on the crushed ice, extracted with ether, ether extract washed with cold sodium carbonate solution and water and dried. Removal of solvent and vacuum distillation of the residue furnished racemic indanone (XXXIX) (1.7613 g), b.p. 85°(bath)/0.7 mm.

Refractive index: n_D^{29} 1.5505.

Analysis: Found: C, 81.56; H, 6.92. $C_{10}H_{10}O$ requires: C, 82.16; H, 6.90%.

I.R. spectrum (liquid film) shows a prominent band at: 1725 cm^{-1}. Other prominent bands at: 2950, 1610, 1460, 1410, 1330, 1260, 1240, 1210, 1150, 1100, 1045, 1025 and 820 cm^{-1}.

G.L.C. The ketone (XXXIX) shows a single peak, retention time 3'17" (polyester column maintained at 220°, flow rate of hydrogen 0.8 ml/sec.).

(±) 3-Methylindan-1-ol (XLI)[35]

A solution of ketone (XXXIX) (0.29 g) in dry methanol (50 ml) was treated with sodium borohydride (0.1160 g) at 0° for 1 hr. Acetic acid (0.3 ml) was added to destroy the excess of reagent and the reaction mixture was diluted with water. Most of methanol was removed and the remaining solution was kept in cold. Solid which crystallised out was recrystallised from methanol-water to give (XLI) (0.0778 g), m.p. 65°.

Analysis: The sample of alcohol (XLI) which was used for C and H estimation was sublimed under vacuum (100° (bath)/7 mm.). Found: C, 80.97; H, 8.13. $C_{10}H_{12}O$ requires: C, 81.04; H, 8.16%).

I.R. spectrum (in Nujol) shows a prominent band at 3230 cm^{-1}. Other prominent bands at: 1460, 1370, 1335, 1080, 1055, 970 and 758 cm^{-1}.

N.M.R. spectrum shows signals at 8.69 τ (3H, doublet; CH_3 on C-3), 4.98 τ (1H, H attached to C-1) and 2.78 τ (aromatic protons).

1-Ethylenedioxycyclohexane (XLII)[25]

A mixture of cyclohexanone (25 g), benzene (300 ml), ethylene glycol (115 ml) and p-toluenesulphonic acid (1.5 g) was stirred under reflux for 34 hrs. The water separated during the reaction was trapped and separated from time to time. Solid sodium carbonate was added to the reaction

mixture, benzene layer was separated, washed with sodium carbonate solution and dried. Residue obtained after removal of the solvent was fractionated.
Ist fraction (4.19 g), b.p. 150-174°.
2nd fraction (15.86 g), b.p. 174-176.5° was the required ketal (XLII). Lit. value [25] b.p. 174-180°.

Refractive index: n_D^{22} 1.4760.

Analysis: Found C, 67.85; H, 9.97. $C_8H_{14}O_2$ requires: C, 67.57; H, 9.93%.

I.R. spectrum (liquid film) shows prominent bands at: 2960, 1450, 1370, 1335, 1280, 1240, 1170, 1120, 1040, 952, 930, 850, 830 and 770 cm^{-1}.

G.L.C. It shows a single peak, retention time 0'42" (the polyester column at 218°; flow rate of hydrogen 0.95 ml/sec).

1-Ethylenedioxy-2-bromocyclohexane (XLIII)

Solution of ketal (XLII) (12.52 g) in dry tetrahydrofuran (125 ml) was cooled in an ice bath, then phenyltrimethylammonium bromide (33.54 g) was added in one lot and the mixture was allowed to stand for 2 hrs at ice-bath temperature with occasional stirring. It was poured into cold 5% sodium bicarbonate solution (200 ml), extracted with ether, ether extract was washed with water and dried. Residue obtained after removal of ether was fractionated and following fractions were collected:

Ist fraction (2.49 g), b.p. 47-50°/11 mm.
2nd fraction (4.61 g), b.p. 50-60°/10 mm.
3rd fraction (2.85 g.), b.p. 60-62°/9 mm.
4th fraction (4.34 g), b.p. 62-64°/9 mm.

The fourth fraction was redistilled in vacuo to give pure bromoketal (XLIII).[23]

Refractive index: $n_D^{24.5}$ 1.5080.

Analysis. Found: C, 43.86; H, 6.07. $C_8H_{13}O_2Br$ requires: C, 43.45; H, 5.88%.

I.R. spectrum (liquid film; p.165) shows prominent bands at: 2900, 1440, 1350, 1330, 1270, 1225, 1200, 1150, 1125, 1075, 1030, 950, 886, 850, 805, 775 and 715 cm^{-1}.

G.L.C. All four fractions were analysed by G.L.C. (Polyester column at 200°, flow rate of hydrogen 1.1 ml/sec.). First three fractions showed presence of lower-boiling impurities, but fourth fraction showed a single peak, retention time 4'31".

Bromodihydro-ar-turmerone (LI, LII)

Dihydro-ar-turmerone (XIX) (3.0 g) was dissolved in acetic acid (30 ml) and to this solution a small amount of HBr dissolved in acetic acid was added. To the stirred solution, bromine (0.8 ml) in acetic acid (6 ml) was added dropwise at the room temperature. Stirring was continued for another 15 minutes at 40° and excess of bromine destroyed by addition

of ethanol (8 ml). Reaction mixture was diluted with water and extracted with ether. Ether extract was washed with sodium carbonate solution and water, dried and solvent was removed in vacuo (water aspirator used, temperature of the bath did not exceed 40°) to give the bromo-ketone (LI, LII) (3.6800 g).

Refractive index: n_D^{27} 1.5188.

I.R. spectrum (liquid film) shows prominent bands at: 2950, 1710, 1510, 1470, 1360, 1270, 1245, 1110, 1040, 1005, 960, 820, 745 and 720 cm^{-1}.

U.V. spectrum (in ethanol) Shoulders at: 262, 259, 264 and 272 mμ (ε values: 587, 489, 343 and 196 respectively).

G.L.C. It shows a single peak, retention time 7'17" (polyester column maintained at 220°, flow rate of hydrogen 0.75 ml/sec). Under identical conditions dihydro-ar-turmerone has retention time 4'51".

Dehydrobromination of bromodihydro-ar-turmerone (LI, LII)

Bromoketone (LI, LII) (3.5 g) was refluxed with collidine (40 ml) for 12 hrs in an atmosphere of nitrogen, diluted with ether (100 ml) and the collidine salt which separated was filtered off. Filtrate was washed with 10% HCl (3x100 ml) and water (3x100 ml), dried and the solvent was removed. Residue was distilled in vacuo to give dehydrobromination product (1.4972 g), b.p. 120° (bath)/1.5 mm.

Refractive index: n_D^{27} 1.5198

Specific rotation: $(\alpha)_D$ + 28° (c, 10.11% in chloroform). Lit.[2] value $(\alpha)_D$ for ar-turmerone: + 60°.

I.R. spectrum (liquid film) shows prominent bands at: 2950, 1700, 1600, 1520, 1450, 1370, 1305, 1240, 1175, 1150, 1115, 1070, 1010, 950, 900, 815 and 720 cm^{-1}.

U.V. spectrum (in ethanol): λ_{max} 281 mμ (ε 6156) and λ_{max} 230 mμ (ε 8640). Lit.[2] value for ar-turmerone: λ_{max} 230 mμ (ε 10,000).

G.L.C. Product of dehydrobromination was analysed by GLC using polyester column maintained at 220°, flow rate of hydrogen 0.8 ml/sec. It showed three peaks, retention times: 4'36", 7'1", and 8'29". Under same conditions the retention time for dihydro-ar-turmerone (XIX) was 4'39", and for ar-turmerone (III) 7'1".

From the product of dehydrobromination, the 2,4-dinitrophenyl-hydrazone of ar-turmerone (LIII) was prepared according to the method reported in the literature.[21] It was chromatographed over alumina, gr.II and eluted with pet.ether 40-60°, 1:1 mixture of pet.ether 40-60° and benzene, benzene and ethanol.

I.R. spectrum of the fraction eluted with mixture of pet. ether 40-60° and benzene, was identical with the I.R. spectrum of an authentic sample of (LIII).

Ethyl ester of 3-p-tolyl-3-hydroxybutanoic acid (LV)

This ester was prepared from p-methylacetophenone by Reformatsky reaction. A mixture of Zn wool (5.3 g), p-methylacetophenone (10 g) and dry benzene (15 ml) was brought to reflux and bromoethylacetate (11.3 g) in dry ether (15 ml) was added slowly, with stirring. The reaction mixture was refluxed for 1 1/2 hrs, then cooled to 0° and mixed with 10% sulphuric acid (30 ml) with vigorous stirring. Benzene layer was separated, washed with 5% sulphuric acid, 10% sodium carbonate solution and water. Acid washings were combined and extracted with ether, ether extract was washed with water and dried. Removal of the solvent and distillation of the residue furnished the hydroxy ester (LV) (15 g), b.p. $136\text{-}138^{\circ}/4$ mm.

I.R. spectrum (liquid film) shows prominent bands at: 3500 and 1725 cm^{-1}. Other bands at: 3000, 1615, 1515, 1370, 1340, 1280, 1200, 1100, 1030, 960, 925, 850, 820 and 725 cm^{-1}.

Ethyl ester of 3-p-tolylbut-2-enoic acid (LVI)

The hydroxy ester (LV) (15 g) was dissolved in pyridine (30 ml) and benzene (15 ml) and cooled in an ice bath. $POCl_3$ (10 g) in dry benzene (10 ml) was added dropwise and the reaction mixture stirred at $60\text{-}65^{\circ}$ for 20 min., poured on the crushed ice and extracted with ether. Ether extract was washed with water, 5% HCl, 5% sodium carbonate

solution and again with water. Drying of the ether extract and removal of the solvent gave the residue, which on distillation in vacuo furnished the ethyl ester (LVI) (8 g), b.p. 125-126°/2.5 mm.

I.R. spectrum (liquid film) shows a prominent band at 1725 cm^{-1}. Other bands at: 2950, 1620, 1510, 1440, 1360, 1335, 1270, 1160, 1095, 1040 and 820 cm^{-1},

3-p-Tolylbut-2-enoic acid (LVII)[28]

Ethyl ester (LVI) (4 g) was refluxed with NaOH (5 g) in 50% ethanol (100 ml) for 3 hrs, then cooled, diluted with water and neutralised with dilute HCl to give crystalline acid (LVII). Crystallisation of crude acid from ethanol gave the pure product (2 g), m.p. 133°. Lit. value[28] m.p. 135°.

Analysis: Found: C, 74.52; H, 6.95. $C_{11}H_{12}O_2$ requires: C, 74.97; H, 6.86%.

I.R. spectrum (in Nujol) shows band for acid at 2945 cm^{-1}. Other bands at: 1680, 1600, 1435, 1370, 1330, 1280, 1220, 1205, 1020, 925, 870 and 813 cm^{-1}.

N.M.R. spectrum (in chloroform) shows signals at: 7.61τ (singlet, CH_3 attached to aromatic ring), 7.40τ (doublet, J=1.5c.p.s. ), 3.78τ(vinyl proton) and 0.75τ ($-CO_2H$).

3-p-Tolylbut-2-enoyl chloride (LVIII)

3-p-Tolylbut-2-enoic acid (LVII) (2.6 g) and freshly distilled thionyl chloride (2.6 ml; 75% excess) were heated under anhydrous conditions at 100° for 1 hr with occasional shaking, then excess of thionyl chloride was removed in vacuo to furnish the acid chloride (LVIII) (2.5 g), which was used as such without further purification. IR spectrum indicated the absence of starting material.

Isobutyl ester of 3-p-tolylbut-2-enoic acid (LIX)

To an ice cooled solution of isobutyl magnesium bromide (from 0.64 g. of isobutylbromide and 0.1135 g. of magnesium) (0.0046 mole) in dry ether (10 ml), acid chloride (LVIII) (1 g., 0.0054 g. mole) in dry ether (10 ml) was added dropwise and with stirring. Stirring was continued for another 1 1/2 hrs at 0°, the reaction mixture was decomposed by addition of cold 10% sulphuric acid, and extracted with ether. Residue obtained after removal of ether was diluted with water (20 ml) and heated on the water bath for 2 hrs. It was extracted with ether, ether extract was washed with sodium carbonate solution [to remove acid (LVII) obtained from unreacted acid chloride (LVIII)] and with water, then dried and ether was removed. Residue was distilled in vacuo to give 0.3665 g. of the ester (LIX), b.p. 160° (bath)/ 2 mm.

Analysis: Found: C, 77.84; H, 8.89. $C_{15}H_{20}O_2$ requires: C, 77.55; H, 8.68%.

I.R. spectrum (liquid film; p.166) shows prominent band at 1715 cm^{-1}. Other bands at: 3000, 1625, 1590, 1520, 1470, 1380, 1315, 1270, 1155, 1040, 878 and 818 cm^{-1}.

U.V. spectrum (in ethanol) λ_{max} 272 mμ (ε, 14761).

G.L.C. It gave a single peak, retention time 5'31" (polyester column at 220°, flow rate of hydrogen 0.85 ml/sec.). Under identical conditions, the product of dehydrobromination of bromodihydro-ar-turmerone gave three peaks, retention times: 0'58", 2'42" and 4'9".

N.M.R. spectrum (p.175) is discussed in the theoretical part, Chapter II.

Mixture of ester (LIX) (0.0545 g), KOH (0.2736 g) and ethanol (3 ml) was refluxed for 3 hrs and diluted with water. Ethanol was removed by distillation and the residue was extracted with ether to remove neutral fraction. The aqueous layer was acidified, extracted with ether, washed with water and dried. Removal of solvent furnished 0.0425 g of solid which was recrystallised from ethanol to give the acid (LVII), m.p. and mixed m.p. with an authentic sample 130-132°. The identity of the acid (LVII) obtained by saponification was further confirmed by its I.R.spectrum which was identical with that of an authentic sample.

Cinnamoyl chloride (LXI)[36]

Cinnamic acid (LX) (5 g), m.p. 129-130°, was mixed with freshly distilled thionyl chloride (5 ml; 75% excess) and heated at 100° for 1 hr under anhydrous conditions. Excess of thionyl chloride was removed under reduced pressure to give acid chloride (LXI) (5.387 g). The product was used as such without further purification.

Isobutyl ester of 3-phenylprop-2-enoic acid (LXII)[37]

To an ice cooled solution of isobutyl magnesium bromide (from 3.36 g. of isobutyl bromide and 0.718 g. of magnesium) (0.029 mole) in dry ether (40 ml) cinnamoyl chloride (LXI) (5.3 g., 0.032 mole) in dry ether (30 ml) was added dropwise and with stirring. Stirring was continued at 0° for another 1 1/2 hr and the reaction product was worked up as described for (LIX). It was heated on the steam bath for 2 hrs with water (150 ml), cooled, extracted with ether, ether extract was washed with sodium carbonate solution (from this washings 2.7683 g. of cinnamic acid was recovered) and with water, then dried and ether was removed. Distillation of the residue furnished the ester (LXII) (0.9560 g), b.p. 140° (bath)/2 mm.

Refractive index: n_D^{26} 1.5377.

Analysis. Found: C, 76.43; H, 7.32. $C_{13}H_{16}O_2$ requires: C, 76.43; H, 7.89%.

I.R. spectrum (liquid film; p.167) shows a prominent band at 1720 cm^{-1}. Other prominent bands at: 2950, 1640, 1600, 1475, 1450, 1370, 1320, 1280, 1200, 1075, 1020, 980, 870, 770 and 712 cm^{-1}.

U.V. spectrum (in isopropanol): λ_{max} 272 mμ (ε 24620).

G.L.C. It showed a single peak, retention time 2'31" (polyester column, temperature 220°, flow rate of hydrogen 0.9 ml/sec.).

Under identical conditions, the ketone (LXV) showed a single peak, retention time 2'55". The mixture of ketone (LXV) and ester (LXII) showed two peaks, retention times 2'54" and 2'32" respectively (same conditions).

N.M.R. spectrum (p.176) is discussed in the theoretical part of the same chapter.

2-Methyl-6-phenylhex-5-en-4-one (LXV)

To an ice cooled solution of isobutyl magnesium bromide (from 10 g. of isobutylbromide and 1.82 g. of magnesium) (0.075 moles) in dry ether (60 ml), freshly distilled cinnamaldehyde (1.0 g., 0.0075 mole) in dry ether (10 ml) was added dropwise and with stirring. Stirring was continued for 1 hr at 0° and for another 1 hr the reaction mixture was heated to reflux. The reaction mixture was decomposed at 0° by addition of cold 10% sulphuric acid and extracted with ether. Ether extract was washed with 10% sulphuric acid and water, then dried and solvent was removed to furnish

the alcohol (LXIV) (1.02 g) (strong band at 3330 cm^{-1}). The alcohol (LXIV) (1.0 g) in acetone (15 ml) was oxidised with Jones reagent. It was kept with an excess of reagent for 1 hr at the room temperature, then diluted with water and extracted with ether. Ether extract was washed with sodium carbonate solution and with water, dried and ether was removed. Residue was distilled in vacuo to give the conjugated ketone (LXV) (0.5419 g), b.p. 155° (bath)/7 mm.

Refractive index: n_D^{28} 1.5462.

Analysis. Found: C, 82.30; H, 8.57. $C_{13}H_{16}O_1$ requires: C, 82.93; H, 8.56%.

I.R. spectrum (liquid film; p.168) shows prominent bands at: 2940, 1675, 1600, 1480, 1445, 1350, 1325, 1290, 1185, 1060, 975 and 750 cm^{-1}.

U.V. spectrum (in isopropanol): $\lambda_{max}^{278.5}$ mμ (ε 22274).

G.L.C. It gave a single peak, retention time 2'55" (polyester column at 220°, flow rate of hydrogen 0.9 ml/sec). Under identical conditions, cinnamaldehyde gave a single peak, retention time 1'37".

N.M.R. spectrum (p. 176) has been discussed in the theoretical part of Chapter II.

SUMMARY

A number of optically active indanes (3,6-dimethylindan-1-one; 1-ethylenedithio-3,6-dimethylindan; 1,5-dimethylindan; 3β,6-dimethylindan-1β-ol; 3β,6-dimethyl-1β-acetoxyindan and 3β, 6-dimethyl-1β-benzoyloxyindan) have been prepared from the (+) 3-p-tolylbutanoic acid of established absolute configuration obtained from ar-turmerone through degradation. Optical rotatory dispersion curve of 3β,6-dimethyl-1β-acetoxyindan has been studied. With a view to prepare substituted indanes the cyclisation reactions of the alcohols (2-methyl-4-p-tolylpentane-2-ol; 2-methyl-6-p-tolylheptane-4-ol; 6-p-tolyl-2-methylhept-3-ene-2-ol; 2-methyl-6-p-tolylhept-2-en-4-ol and 2,4-dimethyl-6-p-tolylheptane-4-ol) have been studied.

Oxidation of 6-p-tolyl-2-methylhept-3-ene-2-ol furnished ar-turmerone. An attempt to synthesise 2-isopropylidene cyclohexanone from the bromoketal of cyclohexanone was not successful since the bromoketal did not furnish the corresponding Grignard reagent on treatment with magnesium. Bromination of dihydro-ar-turmerone with molar proportion of bromine and subsequent dehydrobromination with collidine furnished a mixture of ar-turmerone and another ketone which is probably 2-methyl-6-p-tolylhept-5-en-4-one. Reaction of 3-p-tolylbut-2-enoic acid and 3-phenylprop-2-enoic acid

with thionyl chloride and treatment of the resulting product with isobutyl magnesium bromide furnished the isobutyl esters of corresponding acids. Reaction of cinnamaldehyde with isobutyl magnesium bromide furnished 2-methyl-6-phenylhex-5-en-4-ol which on oxidation furnished 2-methyl-6-phenylhex-5-en-4-one.

The benzylidene derivative of ar-curcumone has been cyclised at 110° in the presence of polyphosphoric acid, and the obtained ketone has been reduced to 2,5-dimethyl-9-benzosuberan by Huang-Minlon's method.

Ethyl ester of 1-oxo-indane-3-carboxylic acid, prepared according to the literature method, yielded a complex mixture on sodium borohydride reduction and also in the reaction with methyl magnesium iodide. On sodium borohydride reduction (±) 3-methylindanone furnished crystalline (±)-3-methylindan-1-ol.

REFERENCES

1. P. Crabbe and W. Klyne, Tetrahedron, 23, 3449 (1967).
2. V.K. Honwad and A.S. Rao, Ph.D. Thesis submitted to the University of Poona by V.K. Honwad (1966).
3. J.H. Brewster, J. Am. Chem. Soc., 81, 5483 (1959).
4. C. Djerassi, R.R. Engle and A. Bowers, J. Org. Chem., 21, 1547 (1956).
5. H. Rupe and F. Wiederkehr, Helv. Chim. Acta, 7, 654(1924).
6. Mme Ramart-Lucas and M.J. Hoch, Bull. Soc. Chim. France, 19, 220 (1952).
7. S. Dev, J. Ind. Chem. Soc., 256 (1955).
8. A.R. Pinder and R.A. Williams, J. Chem. Soc., 2778(1963).
9. P. Narasimha Rao and H.R. Gollberg, Tetrahedron, 18, 1251 (1962).
10. J.H. Brewster and J.G. Buta, J. Am. Chem. Soc., 88, 2233 (1966).
11. N.K. Basu, U.R. Ghatak, G. Sengupta and P.C. Dutta, Tetrahedron, 21, 2641 (1965).
12. J.K. Norymberski and G.F. Woods, J. Chem. Soc.,3426(1955).
13. "Hydroboration" by H.C. Brown, p. 97, edited by W.A. Benjamin Inc. (1962).
14. R.O. Roblin, Jr., D. Davidson and M.T. Bogert, J. Am. Chem. Soc., 57, 151 (1935).
15. M.T. Bogert and D. Davidson J. Am. Chem. Soc., 56, 185 (1934).
16. V.K. Honwad, E. Siskovic and A.S. Rao, Ind. J. Chem., 5, 234 (1967).
17. E. Klein and G. Ohloff, Tetrahedron, 19, 1091 (1963); and references cited in 16.
18. "Essential Oils" by E. Guenther, Vol. V, p. 121, D. van Nostrand Co.Inc. (1952).

19. R.C. Bansal, J.R. Mottox, E.J. Eisenbraun, P.W.K. Flanagan and A.B. Carel, J. Org. Chem., 31, 2716(1966).

20. Huang-Minlon, J. Am. Chem. Soc., 71, 3301 (1949); K.S. Kulkarni and A.S. Rao, Tetrahedron, 21,1172(1965).

21. H. Rupe and A. Gassman, Helv.Chim. Acta, 19, 569(1936).

22. R.P. Gandhi, O.P. Vig and S.M. Mukherji, Tetrahedron, 7, 236 (1959) and the references cited therein.

23. E.W. Garbisch, Jr., J. Org. Chem., 30, 2118(1965).

24. W.S. Johnson, J. Dolf Bass and K.L. Williamson, Tetrahedron, 19, 861 (1963).

25. M.L. Astle, J.A. Zaslowsky and P.G. Lafyatis, Ind. Eng. Chem., 46, 787 (1954).

26. E. Klein and W. Rojahn, Chem. Ber., 97, 2700 (1964).

27. M. Yanagita and A. Tahara, J. Org. Chem., 20,958(1955).

28. R. Stoermer, F. Grimm and E. Laage, Chem. Ber., 50, 975 (1917); G. Schroeter, Chem. Ber., 41, 5 (1908); G. Schroeter, Chem. Ber., 40, 1597 (1907).

29. "Organic Synthesis" edited by A.H. Blatt, Coll. Vol. I, p. 451 (1946).

30. A. Fredga, Chem. Ber., 89, 322 (1956).

31. N.M.R. spectra catalogue, Varian Associates, Palo Alto, California (1962), spectrum No. 251.

32. W. Baker and W.G. Leeds, J. Chem. Soc., 974(1948).

33. C.A. 43, 117h (1949).

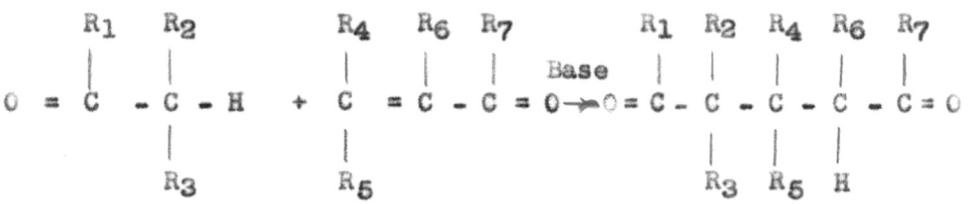
34. E.A. Speight, A. Stevenson and J.F. Thorpe, J. Chem. Soc. (Transactions), 125, 2191 (1924).

35. J.A. Baltrop, R.M. Acheson, P.G. Philpott, K.E. McPhee and J.S. Hunt, J. Chem. Soc., 2936 (1956).

chapter III

transformations of (–) carvone

Michael addition[1] in its original scope is the addition of an addend or donor (A) containing an α-H atom in the system O=C-C-H to a carbon - carbon double bond that forms part of a conjugated system of the general formula C=C-C=O in an acceptor (B).



The condensation takes place under the influence of alkaline reagents. By extension of original scope, Michael condensation has come to be understood to include addends and acceptors activated by groups other than carbonyl and carboxyl. Michael reaction has been widely used for the synthesis of a variety of organic compounds.* As a typical example the Robinson ring annelation,[2] a key reaction for the synthesis of many terpenes and steroids, may be cited.

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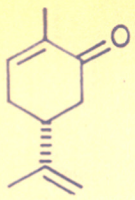
* For review see reference 1.



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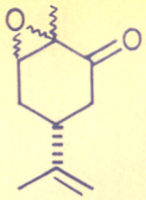

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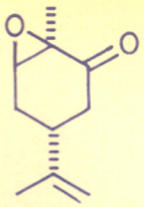

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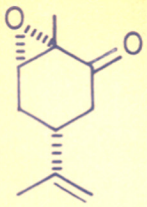

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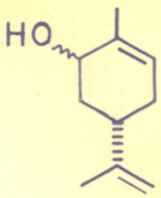

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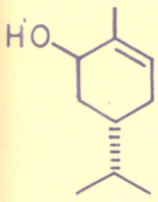

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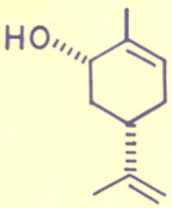

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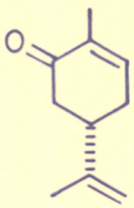

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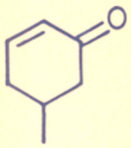

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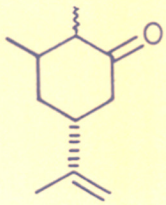

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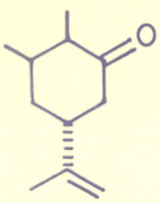

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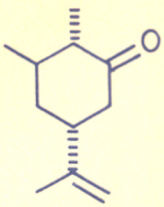

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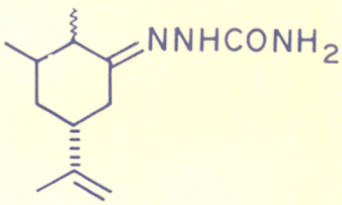

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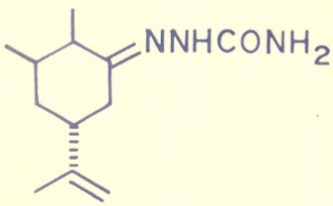

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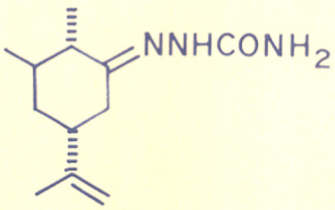

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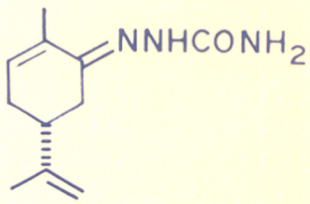

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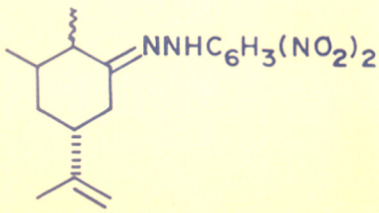

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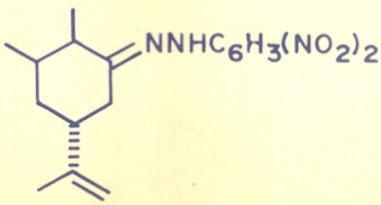

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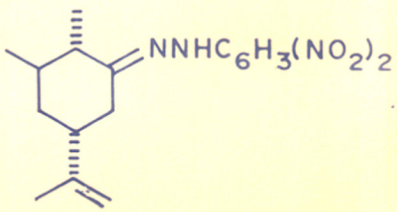

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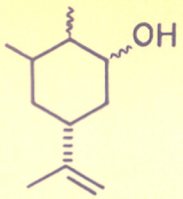

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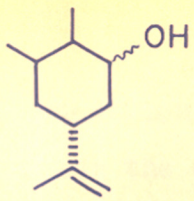

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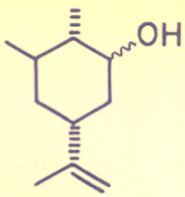

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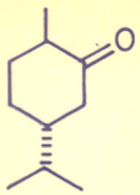

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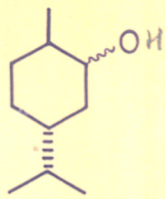
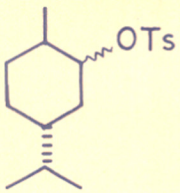
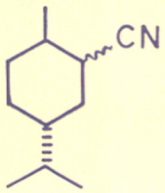


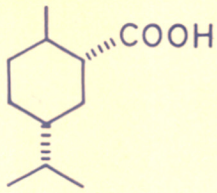
(XX)



(XXI)



(XXII)



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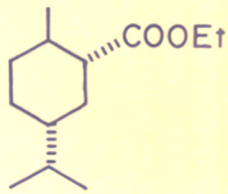

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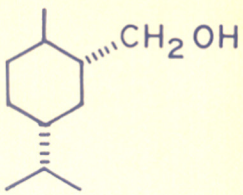
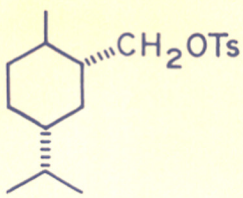
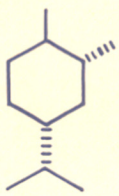


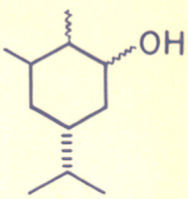
(XXV)



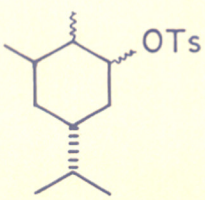
(XXVI)



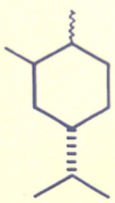
(XXVII)



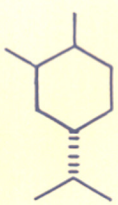
(XXVIII)



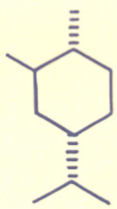
(XXIX)



(XXX)



(XXXI)



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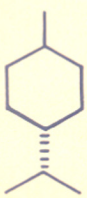
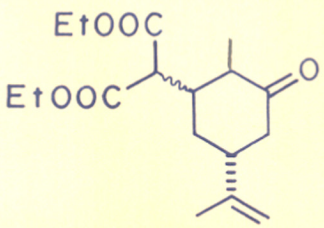
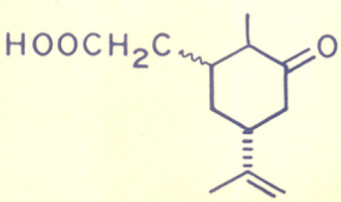


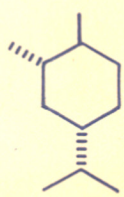
(XXXIII)



(XXXIV)

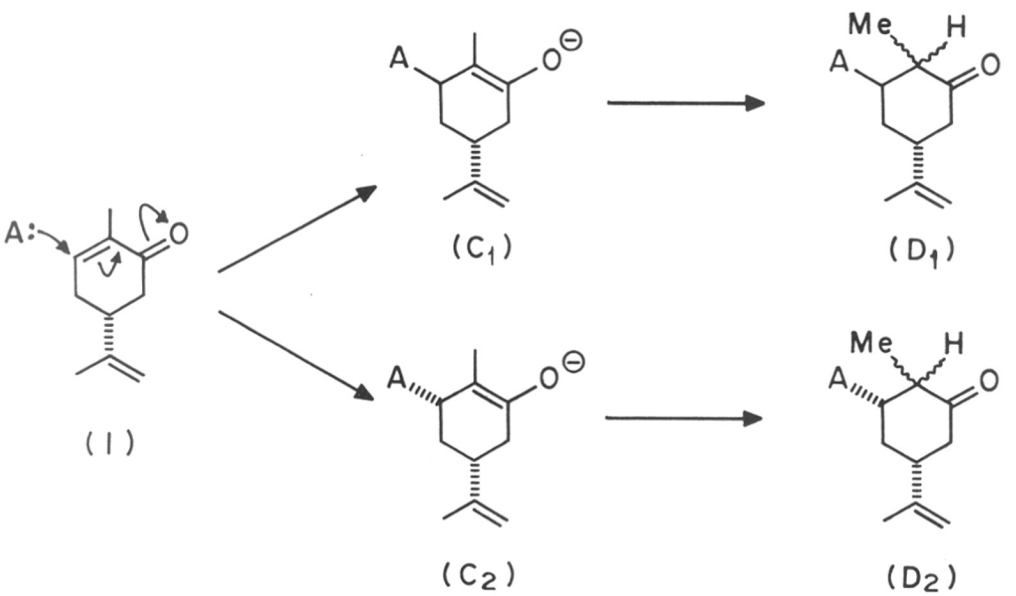


(XXXV)

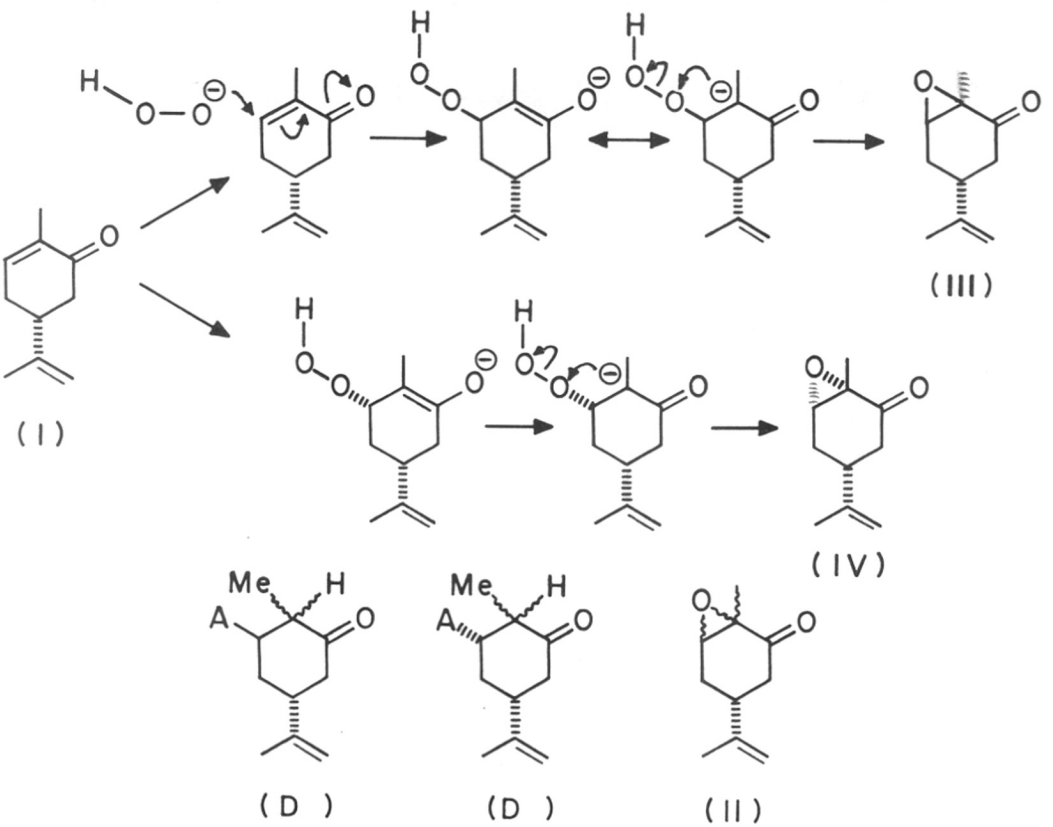


(XXXVI)

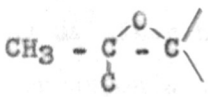
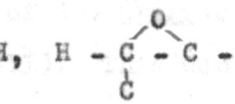
The addition of a nucleophilic reagent to carvone (I) will furnish the enolate (C_1) or (C_2), which will then be transformed to (D_1) or (D_2). The ketones (D_1) and (D_2) have an enolisable hydrogen at the asymmetric centre adjacent to carbonyl group and are capable of epimerisation at C-2 under favourable experimental conditions. Hence in the Michael type of reaction with carvone, the formation of four compounds may be anticipated, two corresponding to

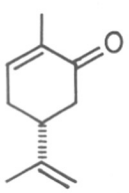


to structure (D_1), (i.e. both the C-2 epimeric ketones) and two corresponding to structure (D_2). However, in the case of addition of $^{\ominus}$O-OH to carvone the number of oxides expected are only two, (III) and (IV). Consequently, we took up the carvone oxide for our investigations. The recently reported reaction involving the hydrazine reduction of α,β-epoxy ketones to allylic alcohols[3-6] has been widely used for the synthesis of steroids and terpenes. Carvone oxide (II)*

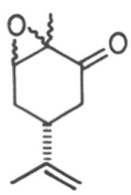


* It will be shown in the sequel that carvone oxide is predominantly (III).

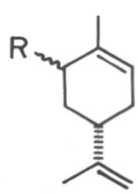
(ν_{max}^{1720} cm^{-1} showing that -C=O group is no longer in conjugation with C=C; U.V. spectrum: no strong absorption at 235 mμ, showing that the conjugated -C=C- of the starting carvone has reacted; ν_{max} 893 cm^{-1} due to  ; N.M.R. spectrum: signals at 8.67 τ (sharp singlet, 3H, ), 8.28 τ (3H, CH_3 attached to double bond), 6.68 τ (multiplet, 1H, ) and 5.27 τ (multiplet, 2H, vinyl protons), on hydrazine reduction furnished the allylic alcohols (VI) and (VII) (ν_{max} 3240 cm^{-1}), which on oxidation furnished (+) carvone (VIII). The sequence (I) → (II) → (V) → (VIII) constitutes an interesting route for the conversion of (-) carvone (I) to (+) carvone



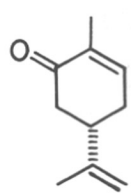
(I)



(II)



(V): R= ξ-OH
(VI): R=β-OH
(VII): R=α-OH



(VIII)

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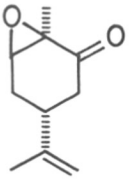
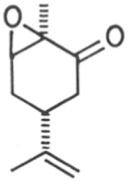
* While our work was in progress we became aware of the recently published investigations of Klein and Ohloff[7] and Schroeter.[8,10]

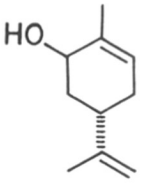
The relative amounts of (III) and (IV) formed during the epoxidation of carvone can be evaluated by knowing the composition of the product obtained on hydrazine reduction. Both the carveols (VI) and (VII) have been properly characterised.[9] The mixture of carveols obtained by us after hydrazine reduction showed $(\alpha)_D$ + 144°, which corresponds to 63.5% of (+) trans-carveol (VI) and 36.5% of (+) cis-carveol (VII). This would suggest that the oxide employed by us for hydrazine reduction is probably a mixture of 63.5% (III) and 36.5% (IV). This conclusion should be regarded as tentative since the yield in the hydrazine reduction, under the conditions employed by us, was rather low (20%). We were considering the modifications of the experimental conditions to increase the yield in the hydrazine reduction; however at this stage we came across the recent publication of Klein and Ohloff[7] who obtained the mixture of carveols in the 45% yield. The carveol mixture so obtained showed $(\alpha)_D$ + 196° corresponding to 91% (VI) and 9% (VII). This would suggest that the carvone oxide is probably a mixture of 91% (III) and 9%



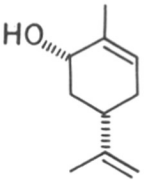
(III)



(IV)



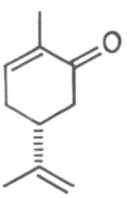
(VI)



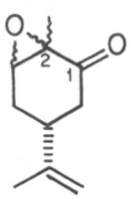
(VII)

(IV).* The carveol mixture (VI and VII) $(\alpha)_D$ + 185.8° obtained by Schroeter[10] by the hydrazine reduction of carvone oxide (II) consisted of 86% (VI) and 14% (VII).

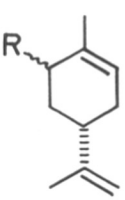
The conjugated addition of cyanide to carvone, initially studied by Lapworth,[11] has been critically examined by Djerassi et al.[12] Three of the four possible addition products have been obtained pure and it has been shown conclusively that addition of cyanide at low temperature furnishes the trans+ addition products (E_1) and (E_2).



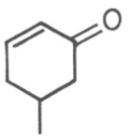
(I)



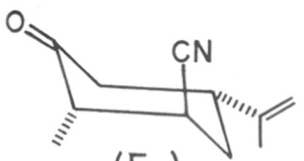
(II)



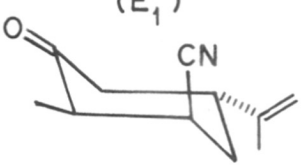
(VI): R=β-OH
(VII): R=α-OH



(IX)



(E_1)



(E_2)

(III): C_2Me-α
(IV): C_2Me-β

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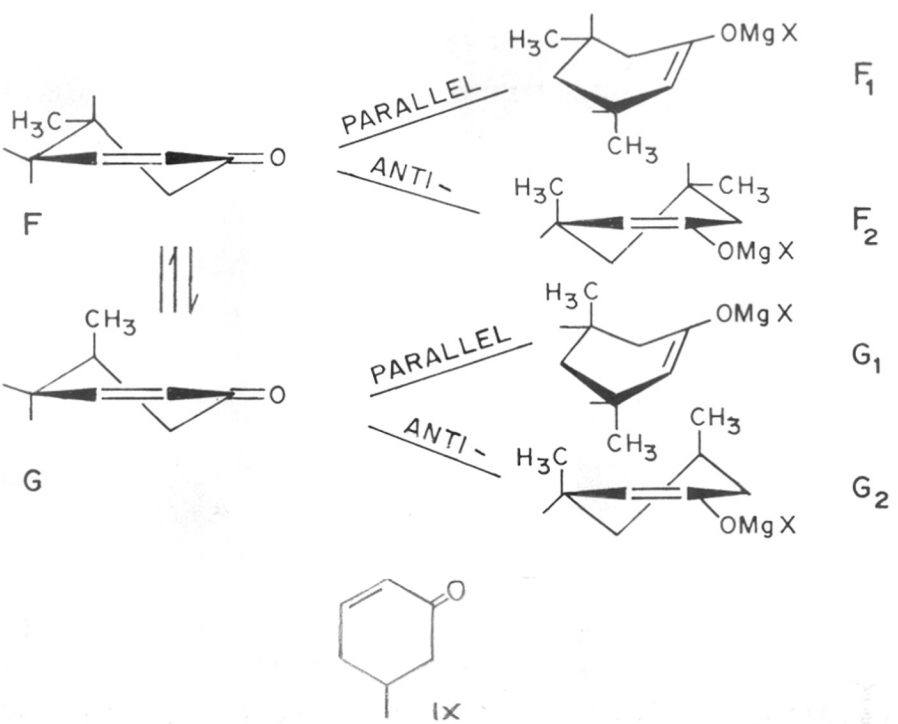
* We consider that in view of the rather low yield of conversion (45%) of carvone epoxide to carveols even under the experimental conditions described by Klein and Ohloff,[7] it is not desirable to infer the composition of the carvone oxide only on the basis of this transformation. However, taking also into consideration the known mode of attack of CN^- on carvone (which results in stereospecific "trans" addition)[12] and particularly the course of 1,4 addition of Grignard reagent to 3-methylcyclohex-5-en-1-one (IX)[13] and the theoretical basis for the steric course of the addition reaction, it can be concluded that epoxidation of carvone (I) furnishes almost exclusively the oxide (III).

+ i.e. incoming CN^- is trans to isopropenyl group.

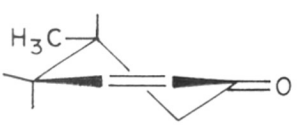
Allinger et al.[13] have studied the 1,4-addition of Grignard reagent to the α,β-unsaturated ketone (IX). They obtained predominantly the trans isomer, which was not clear a priori. Since the above addition reaction is irreversible the product obtained is governed by kinetic control.+ There are two conformations of the cyclohexenone (F) and (G), each of which has 2 possible reaction paths available to it which lead to four different transition states (F_1), (F_2), (G_1) and (G_2), and two different products. Determining factor,



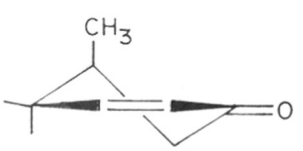
+ The arguments put forth in this paragraph have been taken from the publication of Allinger et al.

as far as stereochemical outcome of reaction, hinges on the relative energies of transition states which result from the four reaction paths. Relative energies of transition states were estimated by examining starting conformations and products. Since parallel attack leads to cyclohexene in boat form and antiparallel attack leads to cyclohexene in chair form, the latter reaction is more likely. Antiparallel attack on conformation (G) gives a transition state in which there is serious interference between two methyl groups. This serious interference is absent in the transition state formed by antiparallel attack on conformation (F). Hence prediction is clear cut and is that reaction should proceed to give the transition state (F_2) leading to the trans isomer as the reaction product.

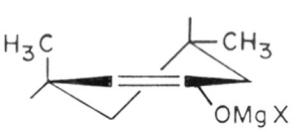
The investigations of Djerassi et al.[12] and Allinger et al.[13] described above prompted us to study some of the addition reactions of carvone (I). Lithium dimethyl



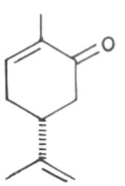
F



G

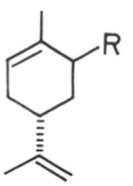


F_2



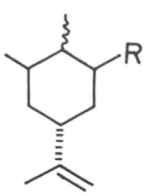
(I)

copper has been found to be very selective in adding a methyl group to the β-carbon of an α,β-unsaturated ketone.[14] Reaction of (-) carvone (I) with lithium dimethyl copper furnished the product (X) [(ν_{max} 1720 cm^{-1} due to -C=O of (X), ν_{max} 1680 cm^{-1} due to -C=O of unreacted carvone (I); λ_{max} 233.5 mμ, ε = 2229 indicating the presence of 26% of unreacted carvone (I); N.M.R. signals at 9.25, 9.12, 9.03 and 8.94 τ (6H, CH_3 on C-2 and C-3), 8.28 τ (CH_3 of isopropenyl group) and 5.28 (2H, vinyl protons)]. The addition product was further characterised through its semicarbazone (XIII), m.p. 182-184°; $(\alpha)_D$ -7°; [$C_{12}H_{21}N_3O$ λ_{max} 226.5 mμ, ε = 17500; no absorption at 265 mμ, indicating the absence of carvone semicarbazone (XIV); N.M.R. signals at 9.11, 9.01, 8.92 and 8.81 τ (6H, CH_3 on C-2 and C-3), 8.30 τ (3H, CH_3 of isopropenyl group), and 5.13 τ (2H, vinyl protons)], and 2,4-dinitrophenyl hydrazone (XV), m.p. 98-99°, $C_{17}H_{22}N_4O_4$. The gas liquid chromatography examination of the addition product (X) showed peaks with retention times of 2'51", 3'6" and 3'41" (polyester column at 180°, flow rate of hydrogen 0.9 ml/sec). The peak at 3'41" corresponds to the retention time of authentic carvone (I), and is hence due to



(I): R=O

(XIV): R=NNHCONH$_2$



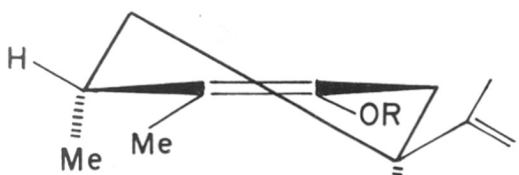
(X): R=O

(XIII): R=NNHCONH$_2$

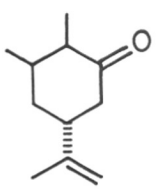
(XV): R=NNHC$_6$H$_3$(NO$_2$)$_2$

unreacted starting material. Since there are two peaks of nearly same intensity in the G.L.C. (besides the peak for the starting material), it is evident that two addition compounds have been formed.

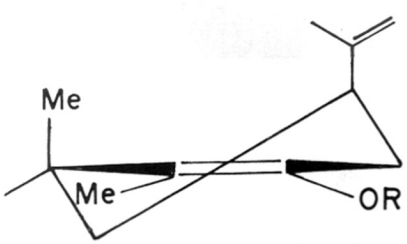
Taking into consideration previous studies on the addition reactions of 3-alkylated cyclohex-5-enones,[13] addition of the methyl group on carvone is expected to take place almost exclusively from the side away from the isopropenyl group since this would involve the transition state (H). Attack from the side cis to the isopropenyl group is not favoured since in the transition state (I) there is serious interference between the methyl and isopropenyl groups. Since C-2 is adjacent to the carbonyl group and has an enolisable hydrogen, the formation of an equilibrium mixture of C-2 epimeric ketones (XI) and (XII) is to be expected under the experimental conditions employed for the



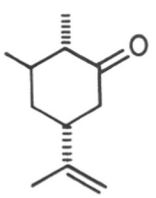
(H)



(XI)



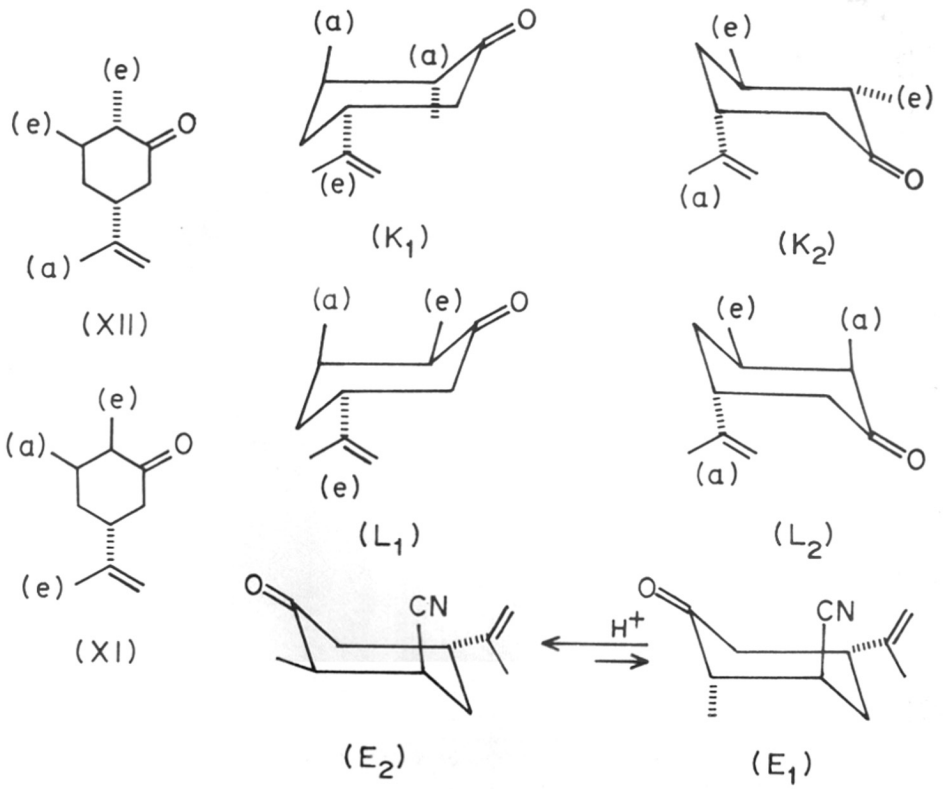
(I) R = CuMeLi



(XII)

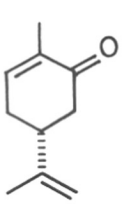
work up of the reaction product. Two chair conformations (K_1) and (K_2) may be considered for the ketone (XII). Since there are two axial methyl groups in conformation (K_1) and only one axial group (isopropenyl) in conformation (K_2), the preferred conformation is (K_2). For the same reason, the chair conformation (L_1) (only one group axial) is to be preferred over the alternate chair conformation (L_2) (two groups are axial). The energy of ketones (XI) and (XII) are expected to be nearly the same and hence on equilibration the mixture will contain approximately equal amounts of (XI) and (XII).

Equilibration of cyanodihydrocarvones (E_1 and E_2) at C-2 has been brought about by keeping the cyanocompound (E_2)

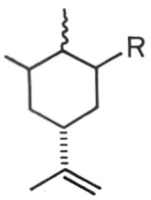


with p-toluenesulphonic acid in ethyl acetate for several days at room temperature.[12] Under identical experimental conditions, the addition product (X) obtained from (-) carvone (I) was recovered unchanged as shown by G.L.C. behaviour, IR spectrum, refractive index and specific rotation. This experiment clearly shows that conditions employed for the work up of (X) are favourable for equilibration at C-2. The formation in almost equal amounts of two C_{11} ketones (X) after reaction of carvone (I) with lithium dimethyl copper and subsequent equilibration at C-2 is consistent with the anticipated stereochemistry at C-3 and the anticipated proportion of C-2 epimeric ketones (XI) and (XII).

Thin-layer chromatography of the C_{11} ketones (X) showed two spots with considerable overlap suggesting that the C-2 epimers have almost identical R_f values. Hence, TLC did not appear attractive for separation of the C-2 epimers on a preparative scale. Since the semicarbazone (XIII),

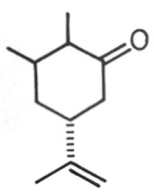


(I)

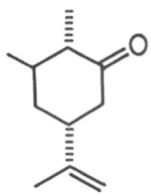


(X) : R=O

(XIII): R=NNCONH$_2$

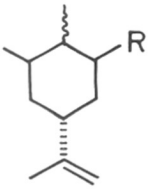


(XI)



(XII)

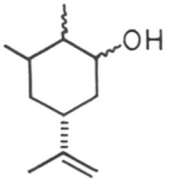
m.p. 182-184°, prepared from the C_{11} ketones (X) was sharp melting, it was considered that it may be derived from one of the two possible C-2 epimers. However, the ketone (X) obtained by regeneration[16] from the semicarbazone (XIII) was also a mixture (approximately 50:50) of C-2 epimers. Probably under the conditions used for regeneration and working up equilibration takes place at C-2.* The product regenerated from the 2,4-dinitrophenyl hydrazone (XV), m.p. 98-99°, was also an equilibrium mixture of C-2 epimeric ketones (X). Lithium aluminium hydride reduction of the C_{11} ketone mixture (X) furnished a mixture of alcohols (XVI), which on T.L.C. examination showed two spots having the R_f values: 0.62 and 0.45. The alcohol(s) R_f = 0.62 on Jones oxidation[15] furnished a C_{11} ketone (R_t on G.L.C. 3'4") free from the C-2 epimer. Similarly the alcohol(s) R_f = 0.45 on Jones oxidation furnished a C_{11} ketone (R_t on G.L.C. 2'51")



(X): R=O

(XIII): R=NNHCONH$_2$

(XV): R=NNHC$_6$H$_3$(NO$_2$)$_2$



(XVI)

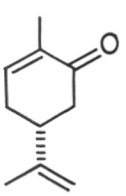
* The experimental observations can also be explained by assuming that the semicarbazone (XIII), m.p. 182-184° is a mixture derived from both the C-2 epimers (X).

free from the C-2 epimer.

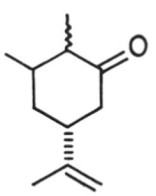
To provide conclusive evidence in support of the C-3 stereochemistry of the C_{11} ketones (X), it was considered desirable to synthesise the hydrocarbon (XXVII). The synthesis of the hydrocarbon (XXVII) has been carried out starting from (-) carvone (I). Hydrogenation of (-) carvone (I) in acetic acid in the presence of platinum on charcoal followed by Jones oxidation[15] of the reaction product furnished tetrahydrocarvone (XIX). (XIX) was converted to the acid (XXIII), m.p. 50-51° (υ_{max} 1710 cm^{-1}; N.M.R. signal at - 0.96τ(due to -COO<u>H</u>), employing the route -

.[17]

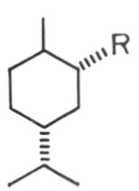
The stereochemistry at C-1, assigned to the acid (XXIII) is based on the reasonable assumption that the carboxylic group is equatorially oriented since the experimental conditions employed for the saponification of nitrile (XXII) are sufficient to establish equilibration at C-1 in the acid (XXIII)



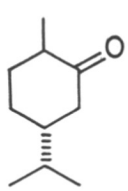
(I)



(X)



(XXIII): R = COOH
(XXVII): R = CH_3

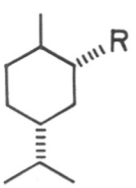


(XIX)

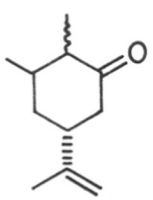
which has a -C = O group adjacent to the asymmetric centre at C-1, carrying a hydrogen atom. The ethyl ester (XXIV) was reduced with lithium aluminium hydride to furnish the alcohol (XXV) [(ν_{max} 3330 cm^{-1} due to -OH, N.M.R. signal at 6.45τ(2H, $-C\underline{H}_2$ - OH)].

The tosylate (XXVI) (ν_{max} 1180 and 1170 cm^{-1}) on reduction with LAH furnished the required hydrocarbon (XXVII) which on G.L.C. examination exhibited a single peak (retention time 1'35", polyester column at 116°, flow rate of hydrogen 0.83 ml/sec).

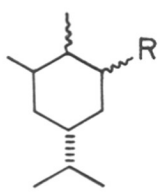
The mixture of C_{11} ketones (X) was hydrogenated using platinum on charcoal catalyst and acetic acid as solvent. The mixture of alcohols (XXVIII) was converted to the tosylates (XXIX) which was reduced with LAH to furnish a mixture of hydrocarbons (XXXI) and (XXXII). The hydrocarbon mixture on GLC analysis exhibited two peaks with retention



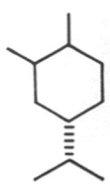
(XXIV): R=COOEt
(XXV) : R=CH_2OH
(XXVI): R=CH_2OTs
(XXVII): R=CH_3



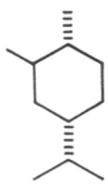
(X)



(XXVIII): R=OH
(XIX): R=OTs



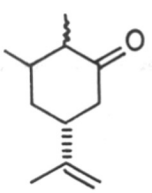
(XXXI)



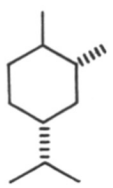
(XXXII)

times 1'56" and 2'14". This suggests that both the components of the hydrocarbon mixture are different from the synthetic C_{11} hydrocarbon (XXVII).* The results are consistent with the assigned C-3 stereochemistry of C_{11} ketones (X).

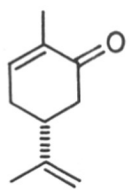
The Michael addition of diethylmalonate to (-) carvone (I) in the presence of NaOEt[18] furnished the addition product (XXXIV) [(ν_{max} 1725 cm^{-1}; N.M.R. signals (see experimental part)]. It appeared attractive to convert



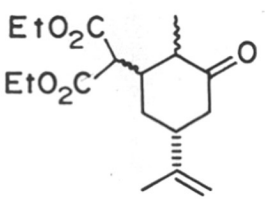
(X)



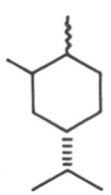
(XXVII)



(I)



(XXXIV)



(XXX)

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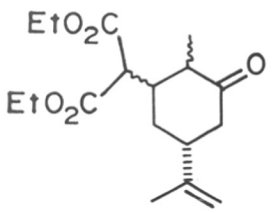
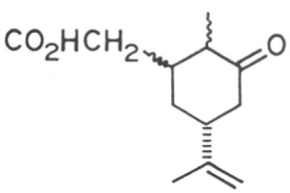
* Because of low yield in the conversion of C_{11} ketones to the C_{11} hydrocarbon mixture (XXX), we had only a limited amount of the C_{11} hydrocarbon mixture. Hence, it has not been possible for us to compare the G.L.C. behaviour of the above hydrocarbon mixture and the synthetic C_{11} hydrocarbon (XXVII) under a variety of experimental conditions.

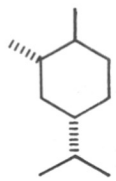
(XXXIV) to the acid (XXXV) which could then be transformed after a number of steps to the C_{11} hydrocarbon (XXXVI). However, an attempt to prepare the acid (XXXV) by acid hydrolysis of (XXXIV) did not prove successful.



(XXXIV)



(XXV)



(XXXVI)

EXPERIMENTAL

5α-Isopropenyl-2ξ-methyl-2,3ξ-oxidocyclohexan-1-one (II)

To a solution of (-) carvone (I) (4.40 g), obtained by fractionation of spearmint oil (fraction having α_D - 55° (neat) in dioxane (175 ml), 30% hydrogen peroxide (15 ml) and 1N NaOH solution (44 ml) were added gradually and the reaction mixture was allowed to stand at the room temperature for 24 hrs. The reaction mixture was diluted with water, extracted with ether (3 x 150 ml), ether extract was washed with water, dried and ether was removed. Distillation of the residue furnished mixture of the oxides (III) and (IV) (3.3 g), b.p. 160°(bath)/7 mm. Lit. value[19] b.p. 120-122°/15 mm.

Refractive index: n_D^{25} 1.4800.

Rotation: α_D + 77° (neat).

Specific rotation: $(\alpha)_D$ + 75° (c, 9.9% in chloroform). Lit. value[19] $(\alpha)_D$ - 83.6° for the enantiomeric material prepared from (+) carvone.

Analysis. Found: C, 72.36; H, 8.99. $C_{10}H_{14}O_2$ requires: C, 72.26; H, 8.49%.

I.R. spectrum (liq. film; p.177) shows bands at: 2975, 1720, 1650, 1450, 1385, 1325, 1120, ~~1045~~, 1045, 990, 953, 893, 815 and 755 cm^{-1}.

U.V. spectrum shows no absorption around 235 mμ.

G.L.C. It showed a single peak, retention time 3'48". Under identical conditions (polyester column at 180°, flow rate of hydrogen 1.5 ml/sec), the starting carvone showed a single peak, retention time 2'38".

N.M.R. spectrum (p.185) shows signals at 8.67τ(sharp singlet, 3H, $CH_3 - \underset{C}{\overset{O}{C}} - C$), 8.28τ (3H, CH_3 attached to double bond), 6.68τ(multiplet, 1H, $H - \underset{C}{\overset{O}{C}} - C - C$) and 5.27 (multiplet, 2H, vinyl protons).

5α-Isopropenyl-2-methyl-2-cyclohexen-1ξ-ol (V)

The mixture of epoxides (III) and (IV) (1 g), isopropyl alcohol (22 ml), 80% hydrazine hydrate (7 ml) and glacial acetic acid (0.3 ml) was heated on the steam bath for 30 minutes and kept at the room temperature for 1 hr. Reaction mixture was diluted with water and extracted with chloroform (3 x 50 ml). The chloroform extract after washing with water, drying, removal of solvent and distillation of the residue, furnished the mixture of (+) carveols (VI) and (VII), (0.20 g), b.p. 150°(bath)/11 mm.

Specific rotation: $(\alpha)_D$ + 144° (c, 4.835 in chloroform). Lit. value[9] $(\alpha)_D$ for (VI) + 213°; lit. value[9] $(\alpha)_D$ for (VII) + 24°. Calculated for 63.5: 36.5 mixture of (VI) and (VII) + 144°.

Analysis: Found: C, 78.56; H, 10.88. $C_{10}H_{16}O_1$ requires: C, 78.89; H, 10.59%.

I.R. spectrum (liquid film; p.178) does not show band in the carbonyl region (1720 cm^{-1}). It shows bands at: 3240, 2880, 1650, 1440, 1370, 1260, 1175, 1060, 1037, 970, 948, 893, 860, 813, 780, 738 and 700 cm^{-1}.

G.L.C. It showed a single peak, retention time 4'41". Under identical conditions (polyester column at 172°, flow rate of hydrogen 1.25 ml/sec) carvone (I) showed a single peak, retention time 4'12".

(+) Carvone (VIII)

The mixture of carveols (VI) and (VII) (0.1603 g) was dissolved in acetone (6 ml) and oxidised by addition of Jones reagent (0.4 ml). The excess of the Jones reagent was destroyed by addition of ethanol (1 ml), the reaction mixture was diluted with water and extracted with ether. Ether extract was washed with water, dried and ether was removed to give (+) carvone (0.1092 g), $(\alpha)_D$ + 45° (c, 3.35% in chloroform), which on distillation in vacuo furnished pure (VIII), b.p. 110°/0.5 mm.

Specific rotation: $(\alpha)_D$ + 53° (c, 2.01% in chlofoform). Lit. value[20] $(\alpha)_D$ + 50°.

I.R. spectrum (liquid film) shows bands at: 2900, 1720, 1680, 1450, 1375, 1255, 1235, 1148, 1118, 1065, 999, 965, 900, 809 and 708 cm^{-1} [(identical with the I.R. spectrum of an authentic sample of (VIII)].

U.V. spectrum (in ethanol): λ_{max} 234 mμ (ε = 8000). Lit.[21] value: λ_{max} 235 mμ (ε = 8510).

G.L.C. (+) Carvone obtained by Jones oxidation of (+) carveol was compared in G.L.C. with an authentic sample of carvone. Conditions: polyester column maintained at 172°, flow rate of hydrogen 1.25 ml/sec. (+) carvone showed a single peak, retention time 4'22", while authentic (I) showed a single peak, retention time 4'18".

5α-Isopropenyl-2,3β-dimethylcyclohexan-1-one (X)[25]

To a cold (0°) solution of lithium dimethyl copper (from 13 g. of copper iodide, 35 g. of methyliodide and 2.8 g of lithium) in dry ether (250 ml) was added dropwise and with stirring a solution of (-) carvone (I) (5 g) in dry ether (100 ml). The reaction mixture was stirred at 0° for 1 hr. and added to ice-cold aqueous ammonium chloride. The reaction product was extracted with ether, ether extract was washed with water, dried and ether was removed. The distillation of the residue furnished the mixture of methyl-carvones (X) and starting carvone (I) (4.2253 g), b.p. 110° (bath)/15 mm.

Refractive index: n_D^{27} 1.4770.

Specific rotation: $(\alpha)_D$ - 31° (c, 21.1% in chloroform).
I.R. spectrum (liquid film; p.179) shows prominent bands at: 2940, 1720, 1640, 1460, 1370, 1260, 1220, 1165, 1080, and 895 cm^{-1} and a weak band at 1680 cm^{-1} indicating the presence of unreacted carvone.
U.V. spectrum (in isopropanol): λ_{max} 233.5 mμ (ε = 2229), which indicates 26% of unreacted starting material.
G.L.C. The reaction product showed three peaks, retention times: 2'51", 3'6" and 3'41" (polyester column at 180°, flow rate of hydrogen 0.9 ml/sec). Under identical conditions, carvone (I) showed a single peak, retention time 3'41".
N.M.R. spectrum (p.185) given in the theoretical part.

Equilibration of C_{11} ketones (XI) and (XII)

Equilibration of C_{11} ketones (XI) and (XII) was carried out according to the method described in the literature. A solution of C-11 ketones (0.4 g) and p-toluenesulphonic acid (0.4 g) in ethyl acetate (9 ml) was kept at the room temperature for 7 days, diluted with water and worked up in the usual way. The product of equilibration was identical with the starting mixture of ketones, since there was no change in refractive index, specific rotation, I.R. spectrum, G.L.C. and T.L.C. behaviour.

5α-Isopropenyl-2ξ,3β-dimethylcyclohexan-1-one semicarbazone[26] (XIII)

A solution of the mixture of ketones, obtained by reaction of lithium dimethyl copper with carvone (X) (1.0025 g) in ethanol (20 ml) was added to the solution of semicarbazide hydrochloride (2 g) and sodium acetate (3 g) in water (20 ml) and the reaction mixture was kept overnight at the room temperature. The solid which crystallised out (1.0673 g) was filtered off and washed with water. It was recrystallised from ethanol to give (XIII) (0.6541 g), m.p. 182-184°.

Specific rotation: $(\alpha)_D$ - 7° (c, 5.187% in acetic acid).

Analysis. Found: C, 64.68; H, 9.53; N, 18.65. $C_{12}H_{21}N_3O_1$ requires: C, 64.54; H, 9.48; N, 18.82%.

I.R. spectrum (in Nujol, p.184) shows bands at: 3450 and 3200 cm^{-1}, which are characteristic for amino group. Other bands at: 2900, 1680, 1560, 1470, 1370, 1105, 1070, 890, 770 and 730 cm^{-1}.

U.V. spectrum: λ_{max} 226.5 mμ (ε = 17500), which is characteristic for the saturated semicarbazones.[22] There was no absorption around 265 mμ, which indicates absence of semicarbazone of α,β-unsaturated ketone.[22]

N.M.R. spectrum (in pyridine) (p.187): given in the theoretical part.

From the mother-liquor was obtained a mixture of semicarbazone (XIII) and carvone semicarbazone (XIV) (0.25 g), m.p. 113-115°.

U.V. spectrum: λ_{max} 228 mμ (ε = 12300) and λ_{max} 260 mμ (ε = 8000).

Regeneration of C_{11} ketones (X) from semicarbazone (XIII)

The mixture of C_{11} ketones (XI) and (XII) was regenerated from semicarbazone (XIII) by the method described in the literature.[16] Semicarbazone (XIII), m.p. 182-184° (0.4852 g) was dissolved in levulinic acid (44 g) containing 10% of 1N HCl and the mixture was magnetically stirred at the room temperature for 20 hrs. The reaction mixture was diluted with water, extracted with ether, ether extract was washed with sodium bicarbonate solution and water, dried and ether was removed. The residue was distilled in vacuo to give the mixture of C_{11} ketones (X) (0.2007 g), b.p. 135°(bath)/12 mm. G.L.C. The obtained product was compared in G.L.C. with the mixture of C_{11} ketones (carbowax column at 171°, flow rate of hydrogen 1.66 ml/sec). It showed two peaks, retention times: 5'48" and 6'20".

Under identical conditions, the product of reaction of carvone with lithium dimethyl copper showed three peaks, retention times 5'45", 6'25" and 7'35" (last peak corresponds to carvone).

2,4-Dinitrophenyl hydrazone of 5α-isopropenyl-2ξ,3β-dimethyl-cyclohexan-1-one (XV)

2,4-DNP derivative of (X) was prepared according to the standard procedure, starting with 0.26 g. of (X). The

product obtained was chromatographed over alumina, gr.II (11 g). The fraction eluted with pet.ether 60-80°(0.2721 g), m.p. 77-81°, was crystallised from benzene-pet.ether 60-80° to give 2,4-dinitrophenyl hydrazone (XV), m.p. 98-99°.

Analysis: Found: C, 58.61; H, 6.59; N, 16.45. $C_{17}H_{22}N_4O_4$ requires: C, 58.94; H, 6.40; N, 16.18%.

I.R. spectrum (in Nujol) shows bands at: 3330 (w), 2950, 1630, 1595, 1500, 1475, 1450, 1375, 1340, 1310, 1270, 1135, 1075, 925, 890, 837, 745 and 725 cm^{-1}.

Light absorption (in chloroform): λ_{max} 356 mμ (ε 23686) (characteristic for the 2,4-dinitrophenyl hydrazones of saturated ketones).[22]

Regeneration of C_{11} ketones from 2,4-dinitrophenyl hydrazone

2,4-DNP derivative (XV) (185 mg), m.p. 98-99°, was dissolved in levulinic acid (18 g) containing 1N HCl (2 ml) and chloroform (8 ml) and the reaction mixture was heated under reflux for 3 hrs, cooled diluted with water and extracted with chloroform. Chloroform extract was washed with sodium bicarbonate solution and with water, dried and solvent was removed. Residue was distilled in vacuo to give mixture of ketones (X) (0.1243 g), b.p. 120°(bath)/20 mm.

I.R. spectrum (liquid film) shows a strong band at 1720 cm^{-1}.

U.V. spectrum (in isopropanol) indicates the absence of carvone (I) (no absorption around 230 mμ).

G.L.C. It showed peaks, retention times 5'45" and 6'19". Under the identical conditions (carbowax column a t 171°, flow rate of hydrogen 1.66 ml/sec), the product of reaction of carvone with lithium dimethyl copper (X) showed three peaks, retention times: 5'45", 6'25" and 7'35" (last peak corresponds to carvone).

5α-Isopropenyl-2ξ,3β-dimethylcyclohexan-1ξ-ol (XVI)

A solution of C_{11} ketones (X) (2.0 g) in dry ether (20 ml) was slowly added to a suspension of LAH (1.38 g., 50% activity) in dry ether (30 ml) kept cooled at 0°. The reaction mixture was then heated to reflux for 1 1/2 hrs, cooled to 0° and the excess of LAH decomposed by addition of technical ether and cold water. Acidification with cold 10% HCl, extraction with ether, washing of the ether extract with sodium carbonate solution and with water, drying and removal of solvent furnished the residue which was distilled in vacuo to give C_{11} alcohols (XVI) (1.5165 g), b.p. 136° (bath)/10 mm.

I.R. spectrum (liquid film) shows a prominent band at 3350 cm^{-1}. Other bands at: 2900, 1640, 1450, 1370, 1030, 1020, 890 and 810 cm^{-1}.

T.L.C. The mixture of alcohols (XVI) gave two separate spots on T.L.C. (solvent system 15% ethyl acetate in pet.ether 60-80°), R_f values: 0.62 and 0.45. The alcohols, R_f 0.62

and R_f 0.45 were separated by preparative T.L.C. (solvent system 15% ethyl acetate in pet.ether 60-80°). Each fraction was dissolved in acetone and oxidised by addition of Jones reagent. The two ketones obtained were analysed by G.L.C.

G.L.C. Polyester column was used, temperature 180°, flow rate of hydrogen 0.9 ml/sec. Ketone obtained by Jones oxidation of alcohol(s), R_f 0.62 gave a single peak, retention time 3'4". Ketone obtained by Jones oxidation of alcohol(s), R_f 0.45 gave two peaks, retention times 2'50" and 3'41". Under identical conditions the mixture of C_{11} ketones (X) and unreacted carvone (I) gave three peaks, retention times: 2'51", 3'6" and 3'41", and the authentic carvone (I) gave single peak, retention time 3'41". I.R. spectrum (liquid film) of the ketone, R_t 3'4", is shown on the page .

Tetrahydrocarvone (XIX)

(-) Carvone (I) (13.7 g) in acetic acid (150 ml) was hydrogenated in the presence of platinum on charcoal catalyst (1.78 g) during 30 hrs at 28° and 711 mm Hg. It absorbed 7000 ml of hydrogen. Catalyst was filtered off and from the filtrate the solvent was removed by distillation under reduced pressure. The residue (no band for the double bond in the I.R. spectrum, strong band for -OH and a weak

one for C=O), was dissolved in acetone (100 ml), cooled to 0° and oxidised by addition of Jones reagent. Excess of the reagent was destroyed by addition of ethanol (2 ml), the reaction mixture was diluted with water and extracted with pet.ether $60-80^{\circ}$. Pet. ether extract was washed with ice-cold 20% NaOH (to remove carvacrol) and with water, dried and solvent was removed. Distillation of the residue furnished (+) tetrahydrocarvone (XIX) (11.71 g), b.p. 110°(bath)/13 mm.

Refractive index: n_D^{28} 1.4545. Lit. value[23] n_D^{20} 1.4552.

Rotation: $\alpha_D + 20^{\circ}$ (neat), Lit.value[23] $\alpha_D - 23^{\circ}$ (neat) for (-) tetrahydrocarvone.

I.R. spectrum (liquid film)shows bands at: 2950, 1720, 1480, 1450, 1430, 1390, 1370, 1250, 1220, 1195, 1175, 1150, 1035, 1020, 1005, 965, 953, 870, 790, 760 and 730 cm^{-1} (identical with that of an authentic sample).

G.L.C. Tetrahydrocarvone (XIX) shows a single peak, retention time 2'17". Under identical conditions (polyester column maintained at 160°, flow rate of hydrogen 1.2 ml/sec) carvone shows a single peak, retention time 3'32".

Tetrahydrocarveol (XX)

A solution of tetrahydrocarvone (XIX) (8.5 g) in dry ether (80 ml) was slowly added to a suspension of LAH (4.566 g., 50% activity) in dry ether (100 ml) which was kept cooled to 0°. The reaction mixture was then heated

under reflux for 2 hrs, cooled to 0° and the excess of LAH was decomposed initially with technical ether and subsequently with cold water. Acidification with 10% HCl, extraction with ether, washing of ether extract with sodium carbonate solution and with water, drying and removal of ether furnished a residue which was distilled in vacuo to give (+) tetrahydrocarveol (XX) (7.887 g), b.p. 130° (bath)/16 mm.

Refractive index: n_D^{27} 1.4600. Lit. value[24] n_D^{22} 1.4634.

I.R. spectrum. (liquid film) shows prominent bands at: 3350, 2900, 1475, 1390, 1370, 1100, 1050, 925 and 840 cm^{-1}.

G.L.C. It shows a single peak, retention time 4'34". Under identical conditions, (+) tetrahydrocarvone (XIX) shows a single peak, retention time 3'45". (Polyester column, temperature 160°, flow rate of hydrogen 1.1 ml/sec).

5α-Isopropyl-2β-methylcyclohexane-1α-carboxylic acid (XXIII)

1. Tosylate of tetrahydrocarveol:

Tetrahydrocarveol (XX) (4.80 g) and p-toluene-sulphonyl chloride (18.07 g) were dissolved in dry pyridine (75 ml) and the reaction mixture was kept at the room temperature for 48 hrs. Dilution with water, extraction with ether, washing with 10% HCl and subsequently with water, drying and evaporation of solvent furnished the crude tosylate (XXI) (10 g). I.R. spectrum (liquid film)

showed the absence of hydroxyl group. It showed bands at 8.4 and 8.5 μ which are characteristic for the tosyl ester.

2. Conversion of tosylate (XXI) to nitrile (XXII)

Crude tosylate of tetrahydrocarveol (XXI) without further purification was used for the preparation of nitrile (XXII). A mixture of (XXI) (10 g), dimethylformamide (535 ml), tert.butanol (295 ml) and KCN (18.1 g) was heated under reflux (140°) for 15 hrs with stirring. The reaction mixture was diluted with water, extracted with ether, ether extract was washed with water, dried and ether was removed to give crude nitrile (XXII) (5 g). The I.R. spectrum of (XXII) showed absence of the bands which are characteristic for tosylate, and presence of the band at 2225 cm^{-1}, which is characteristic for -CN group.

3. Saponification of nitrile (XXII)

Nitrile (XXII) (5 g) was refluxed with 5% glycolic KOH (450 ml) for 6 hrs, diluted with water, cooled to 0° and acidified by addition of conc. HCl. It was then extracted with ether and the ether extract was washed with sodium carbonate solution. The carbonate washings were combined, extracted with ether (to remove completely the neutral fraction), cooled to 0°, acidified by addition of conc. HCl,

extracted with ether, ether extract washed with water and dried. Removal of the solvent and distillation of the residue furnished the acid (XXIII) (0.64 g), b.p. 142° (bath)/1 mm. The acid (XXIII) solidified on keepinga at the room temperature for 12 hrs. It was recrystallised from pet. ether 60-80° to give (XXIII), m.p. 50-51°.

Specific rotation: $(\alpha)_D$ - 10° (c, 10% in chloroform).

Analysis: Found: C, 71.36; H, 10.96. $C_{11}H_{20}O_2$ requires: C, 71.74; H, 10.89%.

I.R. spectrum (in Nujol; p.182) shows prominent bands at: 2950, 1710, 1470, 1450, 1370, 1290, 1240, 1205, 1150, 1025, 943 and 690 cm^{-1}.

N.M.R. spectrum (p.186) shows signal at -0.96 due to -COOH).

Ethyl ester of (XXIII) was prepared by azeotropic method. The product (XXIV), b.p. 110° (bath)/3.5 mm. showed a strong band at 1725 cm^{-1} in its I.R. spectrum (liquid film). Other prominent bands at: 2950, 1440, 1370, 1175, 1140, 1030 and 750 cm^{-1}.

5α-Isopropyl-2β-methylcyclohexane-1α-methanol (XXV)

A solution of ester (XXIV) (0.40 g) in dry ether (10 ml) was added to the ice cooled suspension of LAH (0.50 g) in dry ether (20 ml). The reaction mixture was refluxed for 2 hrs and then cooled in an ice bath and treated carefully

with ice-water to decompose excess of LAH. It was acidified with 10% HCl, extracted with ether, ether extract was washed with sodium carbonate solution and with water, dried and ether was removed. Distillation of the residue furnished alcohol (XXV) (0.2534 g), b.p. 100° (bath)/3 mm.

Specific rotation: $(\alpha)_D$ - 18° (c, 10.05% in chloroform).

Analysis: Found: C, 77.20; H, 12.88. $C_{11}H_{22}O_1$ requires: C, 77.57; H, 13.02%.

I.R. spectrum (liquid film; p.183) shows a prominent band at 3330 cm^{-1}. Other bands at: 2920, 1750, 1700, 1450, 1440, 1375, 1360, 1180, 1135, 1100, 1065, 1035, 1010, 968, 940, 920 and 885 cm^{-1}.

G.L.C. It showed a single peak, retention time 4'14" (polyester column maintained at 180°, flow rate of hydrogen 1.1 ml/sec).

N.M.R. spectrum (p.186) shows signal at 6.45 (2H, -$\underline{CH_2}$ - OH).

4α-Isopropyl-1β,2α-dimethylcyclohexane(XXVII)[27]

A solution of the tosylate of 5α-isopropyl-2β-methylcyclohexane-1α-methanol (XXVI) (0.369 g) [prepared according to the procedure described for tosylate of tetrahydrocarveol (XXI)] in dry ether (10 ml) was added to the ice cooled suspension of LAH (0.322 g) in dry ether (20 ml).

It was refluxed for 8 hrs, then dry 1,2-dimethoxy ethane was added to the reaction mixture to increase its boiling point to 60° (bath temperature). Refluxing was continued for another 8 hrs at 60°, reaction mixture was cooled in ice and the excess of LAH was destroyed by careful addition of cold water. It was acidified by addition of 10% HCl, then extracted with ether, ether extract was washed with sodium carbonate solution and with water, dried and ether was removed (fractionating column was used). The I.R. spectrum of the residue did not indicate presence of the tosylate. Residue, obtained after removal of the solvent was chromatographed over alumina, gr.I (10 g). Elution with pet.ether 60-80°, removal of the solvent and vacuum distillation of the residue, furnished the hydrocarbon (XXVII) (0.0267 g), b.p. 120°(bath)/20 mm.

I.R. spectrum (liquid film) shows bands at: 2950, 1470, 1375, 1280, 1175 and 730 cm^{-1}.

G.L.C. It shows a single peak, retention time 1'51". Under identical conditions (polyester column, temperature 116°, flow rate of hydrogen 1.2 ml/sec), p-menthane (XXXIII) shows a single peak, retention time 1'27".

Molecular weight. The molecular weight (154) was determined through mass spectrum.

Mixture of C_{11} hydrocarbons (XXXI) and (XXXII)

1. Hydrogenation of mixture of C_{11} ketones (XI) and (XII). Mixture of C_{11} ketones (X) (1.5185 g), [obtained by reaction of carvone with lithium dimethyl copper] in acetic acid (20 ml) was hydrogenated in the presence of platinum on charcoal catalyst (0.4323 g) during 26 hrs at 26° and 710 mm. It absorbed 600 ml of hydrogen. Catalyst was filtered off, and from filtrate the solvent was removed by distillation under reduced pressure. Distillation of the residue furnished the mixture of saturated alcohols (XXVIII) and tetrahydrocarveols (XX) (1.0334 g), b.p. 125° (bath)/12 mm. IR spectrum (liquid film) shows a prominent band for -OH (3400 cm^{-1}) and does not show bands in the carbonyl region. G.L.C. It shows three peaks, retention times: 2'17", 2'47" and 3'12" (polyester column, temperature 170°, flow rate of hydrogen 1.1 ml/sec).

2. Mixture of the tosylates of above alcohols.

The tosylates were prepared according to the procedure described for (XXI).

3. LAH reduction of the mixture of tosylates.

Mixture of the tosylates (XXIX) (1.429 g) was dissolved in dry ether (50 ml) and added to an ice cooled suspension of LAH (1.0 g) in dry ether (50 ml). The reaction was carried out as described for (XXVII). The product obtained

after refluxing the reaction mixture for 20 hrs, was the mixture of hydrocarbons (XXXI) and (XXXII), which was chromatographed over alumina, gr.II, eluted with pet.ether 60-80° and distilled after removal of the solvent. Distillation furnished (XXXI) and (XXXII) (0.140 g), b.p. 94° (bath)/16 mm.

G.L.C. It showed peaks, retention times 1'56" and 2'14" due to hydrocarbon mixture (polyester column maintained at 116°, flow rate of hydrogen 1.2 ml/sec). Under identical conditions hydrocarbon (XXVII) showed a single peak, retention time 1'35" and p-menthan (XXXIII) showed a single peak, retention time 1'15".

Diethyl ester of 5α-isopropenyl-2β-methyl-3-oxocyclohexyl malonic acid (XXXIV)

(-) Carvone (I) (3.0 g) was added dropwise to a solution of diethylmalonate (4 g) in absolute ethanol(8 ml) containing sodium (0.2 g), which was cooled in ice and stirred. Addition required 30 minutes, after which the reaction mixture was allowed to come to the room temperature during 2 hrs. The reaction mixture was acidified by addition of acetic acid (0.5 ml), ethanol was removed by distillation under reduced pressure, the residue was diluted with water and extracted with ether. Ether extract was washed with water, dried and ether was removed. The residue was fractionated to give (XXXIV) (3.1673 g), b.p. 174°(bath)/0.5 mm.

Refractive index: n_D^{27} 1.4720.

Specific rotation: $(\alpha)_D$ - 11° (c, 6.383% in chloroform).

Analysis: Found: C, 66.25; H, 8.63. $C_{17}H_{26}O_5$ requires:
C, 65.78; H, 8.44%.

I.R. spectrum (liquid film) p. 184 shows prominent bands at: 2950, 1725, 1640, 1440, 1370, 1280, 1085, 1025, 980, 895 and 862 cm^{-1}.

U.V. spectrum (in isopropanol) does not show absorption around 235 mμ.

T.L.C. It gave a single spot, R_f value 0.50 (solvent system: 6% ethyl acetate in benzene).

N.M.R. spectrum (p.187) shows signals at: 9.03τ (3H, doublet, J=7 c.p.s., CH_3 on C-2), 8.72τ (6H, triplet, CH_3 - CH_2-O), 8.23τ (3H, CH_3 group on double bond), 5.80τ (4H, quadruplet, CH_3 - CH_2- O) and 5.23τ (2H, vinyl protons).

Equilibration experiments:

1. Equilibration was carried out by keeping the reaction mixture at the room temperature for 7 days before acidifying it and working it up. The reaction product obtained by this method was identical to the (XXXIV) obtained by the reaction which lasted 2 1/2 hrs (conclusion has been drawn on the basis of comparison of I.R. spectra, refractive indexes, specific rotations and T.L.C. behaviour).

2. Equilibration was done by keeping the ester (XXXIV) and an equal weight of p-toluenesulphonic acid in ethyl acetate solution at the room temperature for 7 days. The obtained product and (XXXIV) before equilibration had identical I.R. spectra, refractive indexes, specific rotations and T.L.C. behaviour.

S U M M A R Y

(-) Carvone has been transformed to its enantiomer (+) carvone, by preparing the epoxide of (-) carvone, hydrazine reduction of epoxide to (+) carveols and oxidation of (+) carveols to (+) carvone.

Conjugate addition of lithium dimethyl copper to (-) carvone furnished in excellent yield the C-11 ketones, 5α-isopropenyl-2α,3β-dimethylcyclohexan-1-one and 5α-isopropenyl-2β,3β-dimethylcyclohexan-1-one, purified through semicarbazone and 2,4-dinitrophenyl hydrazone. Reduction of C-11 ketone mixture with LAH furnished a mixture of alcohols which could be separated through preparative T.L.C., oxidation of T.L.C. pure C-11 alcohols gave the corresponding C-11 ketones.

Taking into account previous studies on the addition of CN^- to carvone and also the conjugate addition of methyl magnesium iodide to 3-methylcyclohex-5-enone, it has been suggested that the product obtained during the present investigation has the methyl group at C-3 trans to the isopropenyl group at C-5. The formation of two ketones in nearly equal amounts has been explained on the basis of equilibration at C-2 which is adjacent to the C=O group.

4α-Isopropyl-1β,2α-dimethylcyclohexane has been prepared after several steps starting with tetrahydrocarvone, and has been compared in G.L.C. with the mixture of

4α-isopropyl-1β,2β-dimethylcyclohexane and 4α-isopropyl-1α, 2β-dimethylcyclohexane, obtained from the mixture of C-11 ketones.

The diethyl ester of 5α-isopropenyl-2ξ-methyl-3-oxocyclohexylmalonic acid was prepared by addition of malonic ester to (-) carvone in the presence of sodium ethoxide.

REFERENCES

1. "Organic reactions", Vol. 10, p. 179, John Wiley and Sons, Inc. (1959).

2. E.C. De Feu, F.J. McQuillin and R. Robinson, J. Chem. Soc., 53 (1937).

3. P.S. Wharton and D.H. Bohlen, J. Org. Chem., 26, 3615 (1961).

4. C. Djerassi, D.H. Williams and B. Berkoz, J. Org. Chem., 27, 2205 (1962).

5. A. Nickon and W.L. Mendelson, Canad. J. Chem., 43, 1419 (1965).

6. T. Nakano and M. Hasegawa, Chem. Pharm. Bull., 12, 971 (1964).

7. E. Klein and G. Ohloff, Tetrahedron, 19, 1091 (1963).

8. S.H. Schroeter and E.L. Eliel, J. Org. Chem., 30, 1 (1965).

9. R.G. Johnston and J. Read, J. Chem. Soc., 233 (1934).

10. S. Schroeter, Annalen der Chemie, 674, 118 (1964).

11. A. Lapworth, J. Chem. Soc., 89, 945, 1819 (1906);
A. Lapworth and V. Steele, J. Chem. Soc., 99, 1877 (1911).

12. C. Djerassi, R.A. Schneider, H. Vorbrueggen and N.L. Allhuger, J. Org. Chem., 28, 1632 (1963).

13. N.L. Allinger and C.K. Riew, Tetrahedron Letters, 1269 (1966).

14. H.O. House, W.L. Respess and G.M. Whitesides, J. Org. Chem., 31, 3128 (1966).

15. C. Djerassi, R.R. Engle and A. Bowers, J. Org. Chem., 21, 1547 (1956).

16. C.H. DePuy and B.W. Ponder, J. Am. Chem. Soc., 81, 4629 (1959).

17. R.K. Mathur and A.S. Rao, Tetrahedron, 23, 1259(1967).

18. J. Meinwald and E. Frauenglass, J. Am. Chem. Soc., 82, 5235 (1960).

19. N. Treibs, Chem. Ber., 65, 1314 (1932).

20. T.G. Halsall,D.W. Theobald and K.B. Walshaw, J. Chem. Soc., 1029 (1964).

21. Y.R. Naves and P. Bachmann, Helv. Chim. Acta, 29, 62 (1946); H. Mohler, Helv.Chim. Acta, 20, 291 (1937).

22. 'Ultraviolet and visible spectroscopy' by C.N.R. Rao, p. 31, Butterworths (1961).

23. J. Read and R.G. Johnston, J. Chem. Soc., 229 (1934).

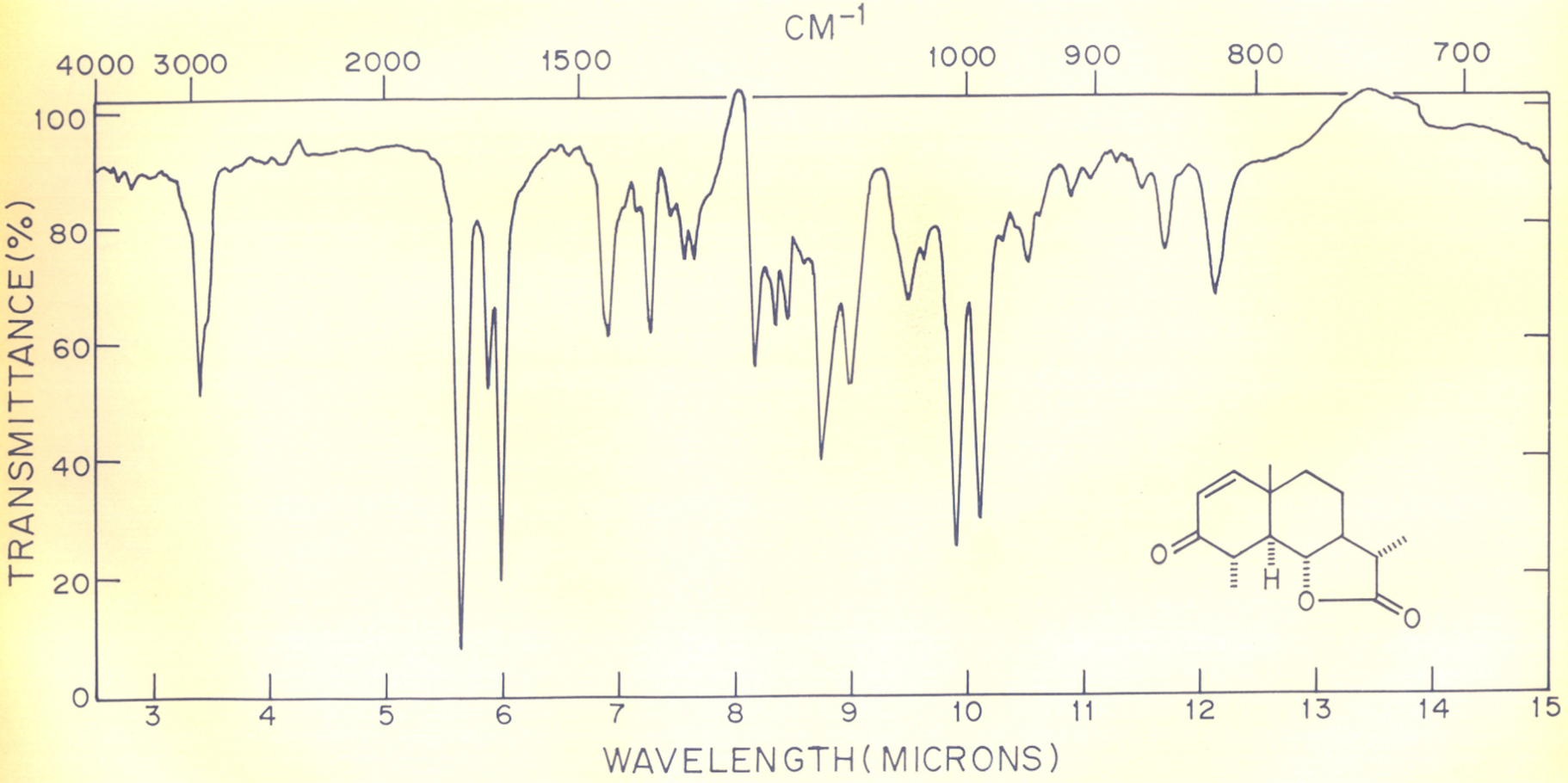
24. R.G. Johnston and J. Read, J. Chem. Soc., 1138(1935).

25. M. Freund and F. Mayer, Chem. Ber., 39, 1122 (1906).

26. same as 25, p. 1124.

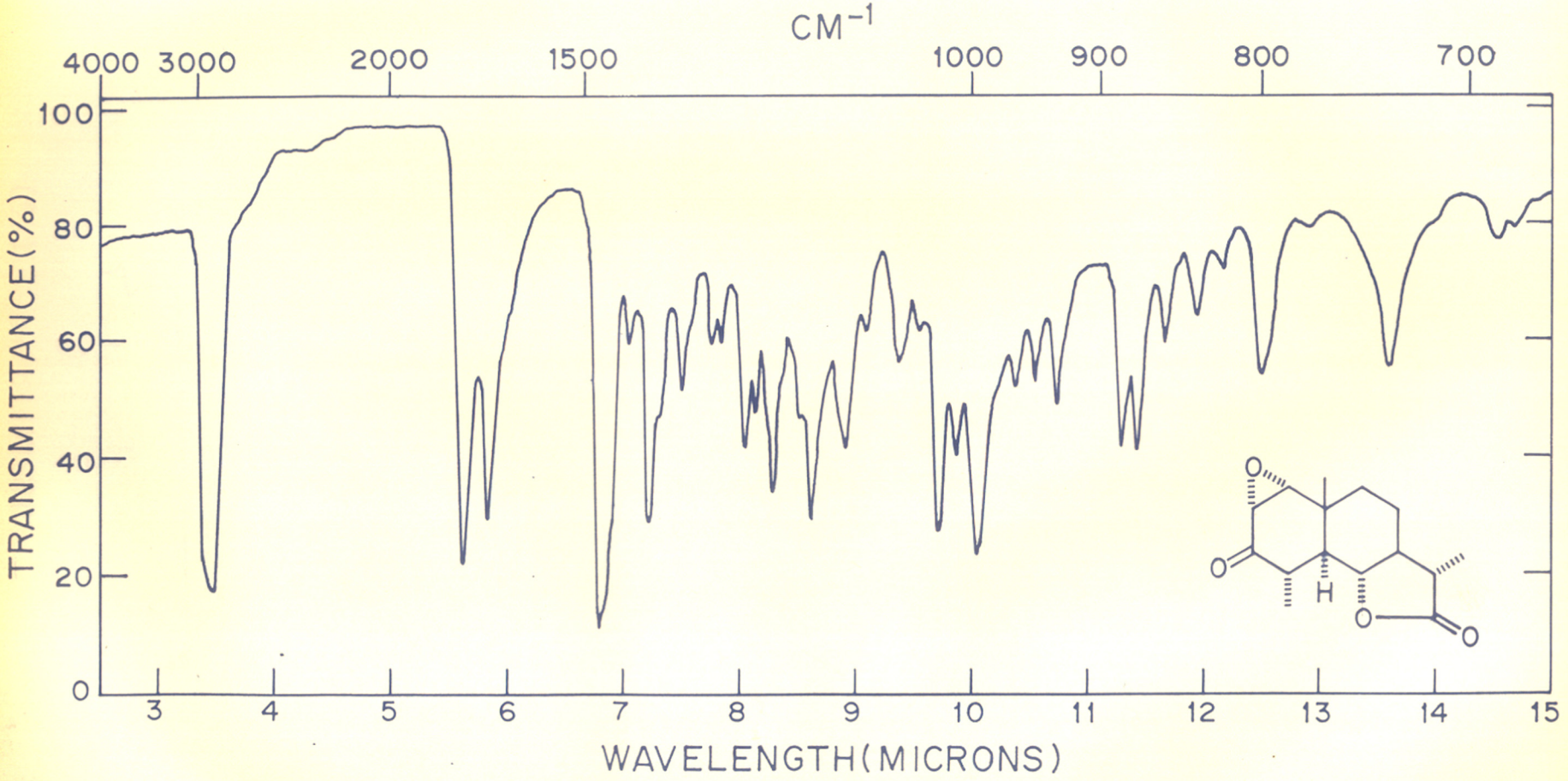
27. G. Clement, Bull.Soc. Chim. France, 229 (1956).

CHAPTER I



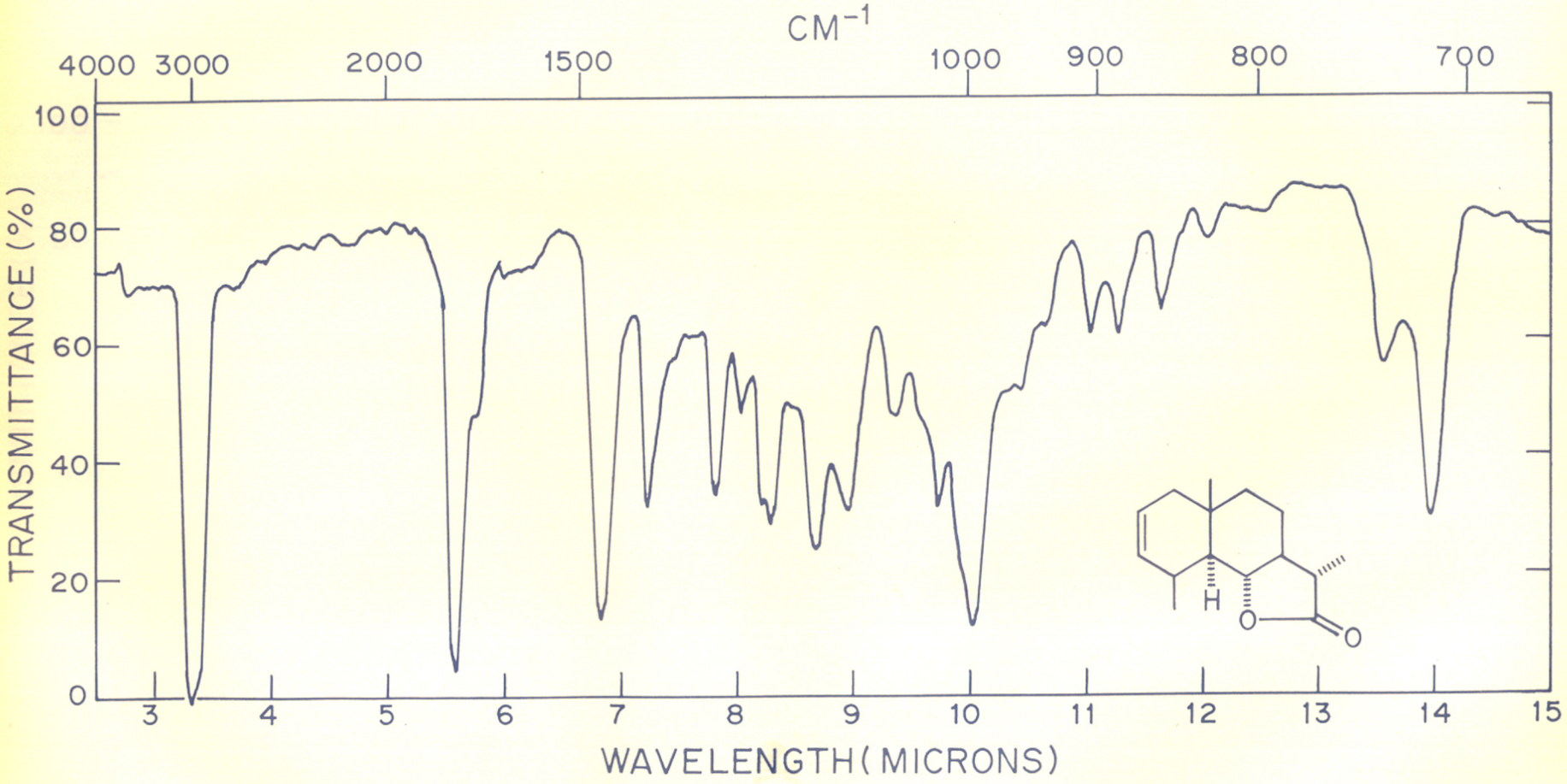
IR SPECTRUM OF 3-OXO-5,7 α (H),4,6,11β(H)-EUDESM-1-EN-6,13-OLIDE (VIII)

(IN CH_2Cl_2 SOLUTION, THICKNESS OF THE CELL: 0·2 mm)



IR SPECTRUM OF 1α,2α-OXIDO-3-OXO-5,7,α(H),1,2,4,6,11β(H)-EUDESMAN-6,13-OLIDE (XV)

(IN NUJOL)



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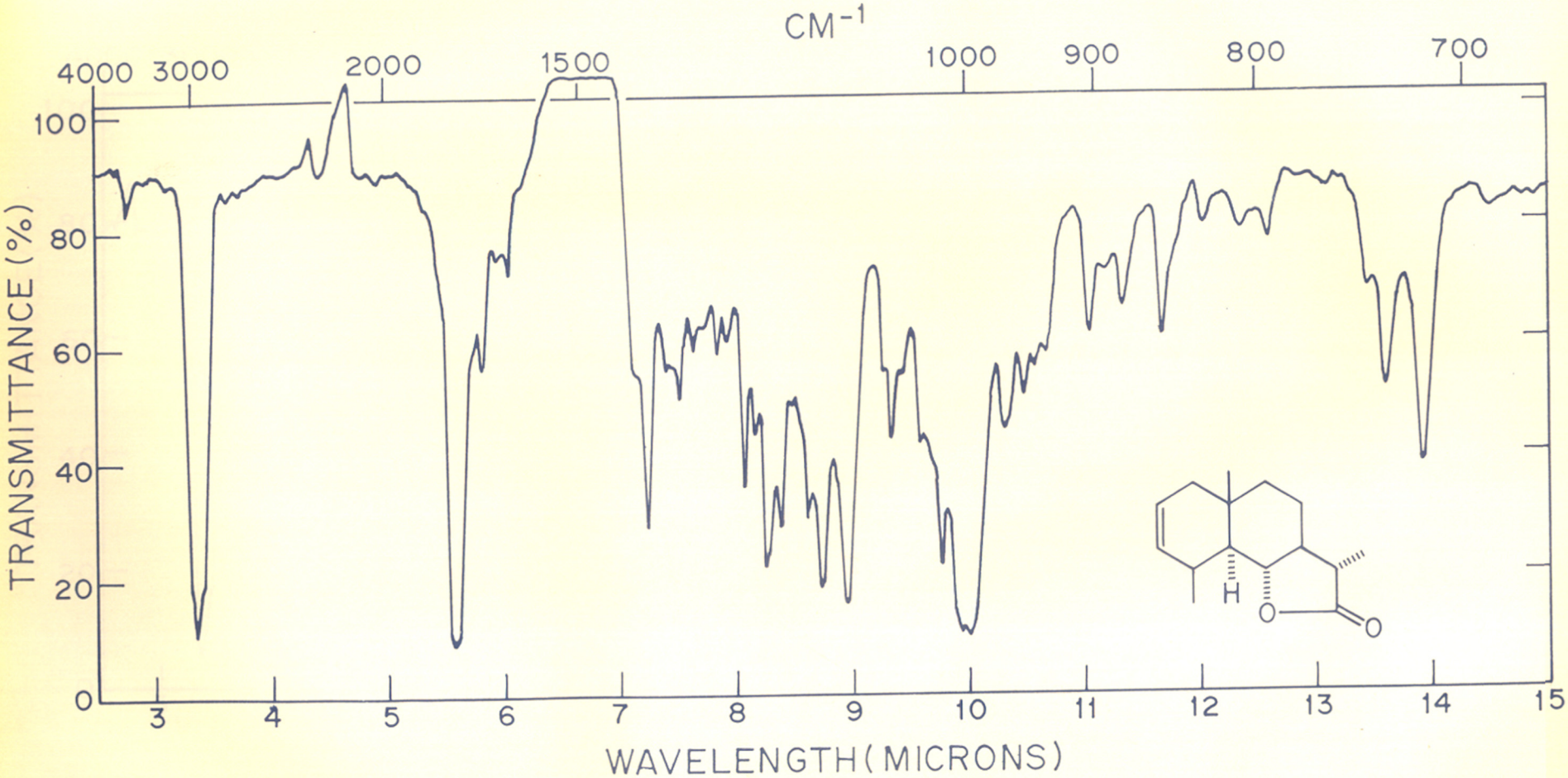
(IN NUJOL)



IR SPECTRUM OF 4,5 α (H), 6,11 β (H)-EUDESM-2-EN-6,13-OLIDE (XIX)

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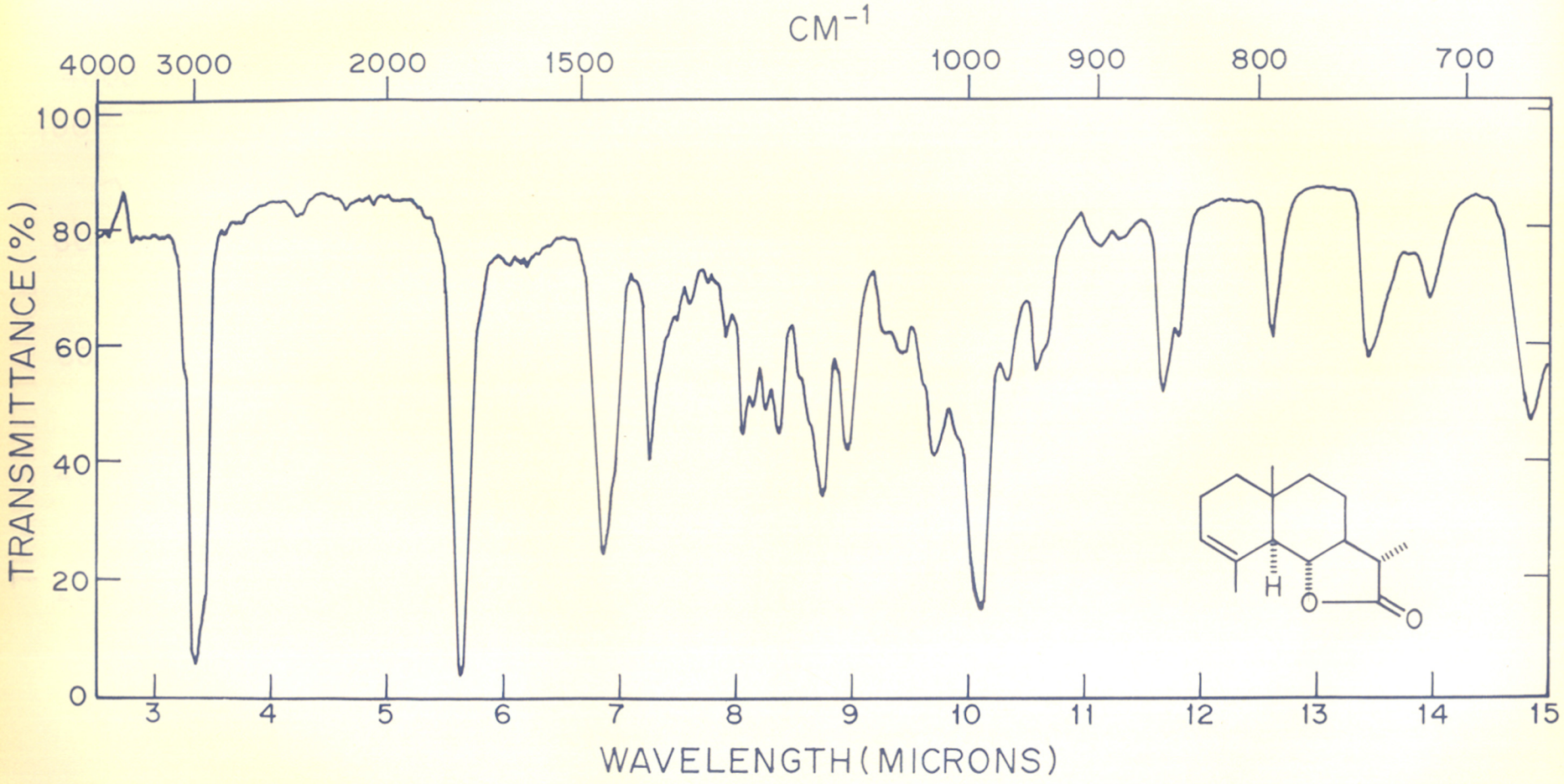

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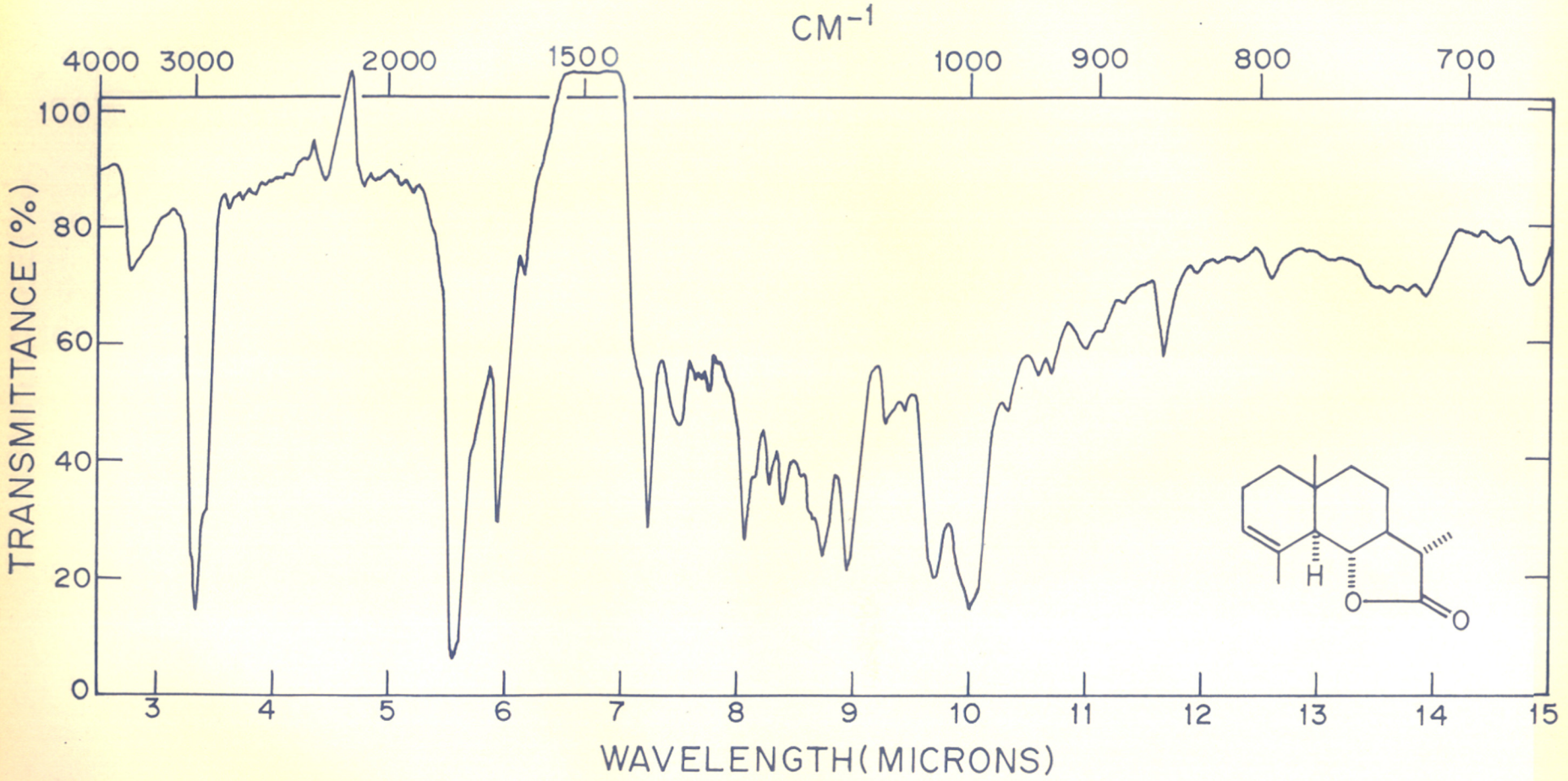
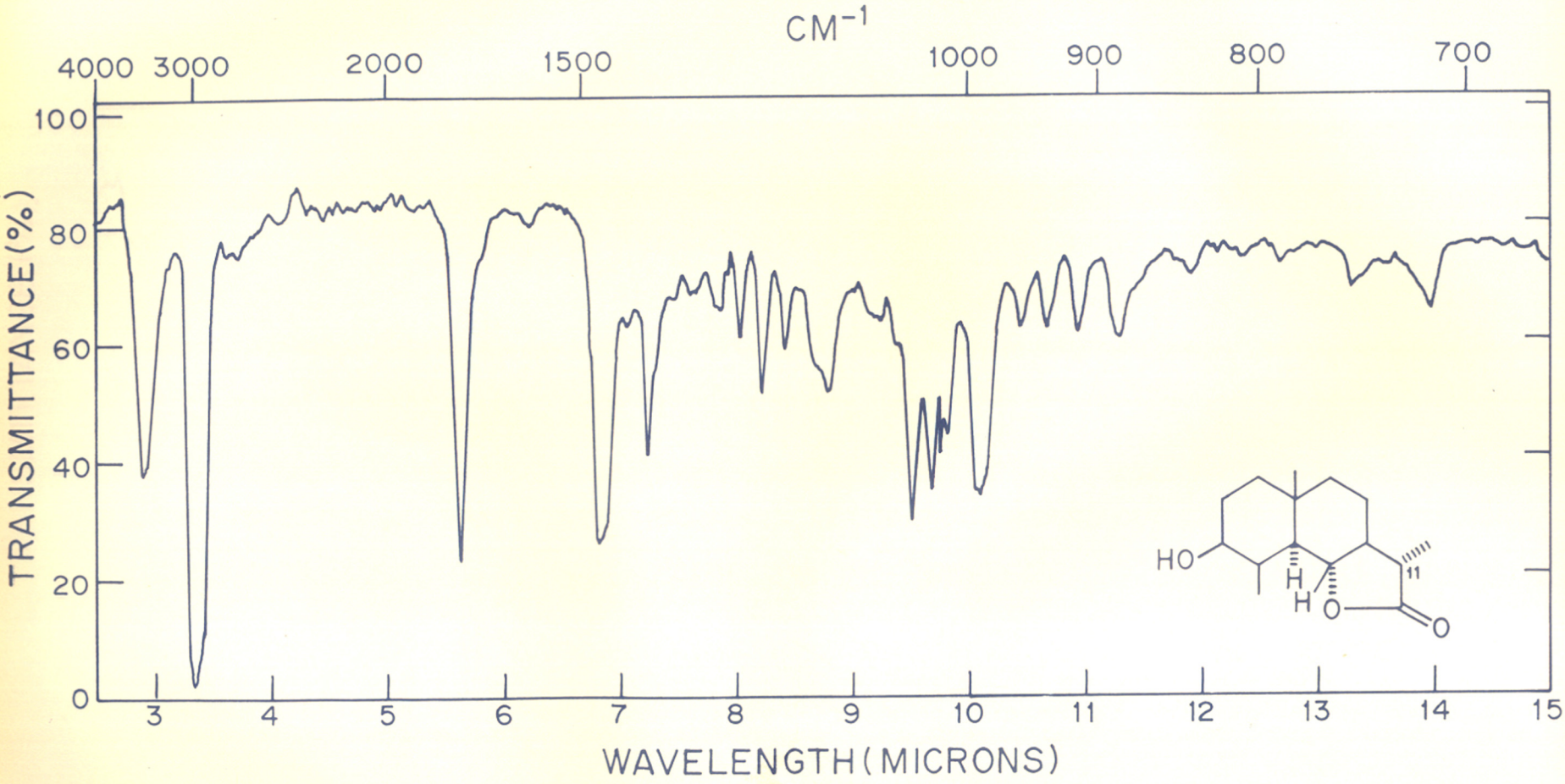
(IN NUJOL)



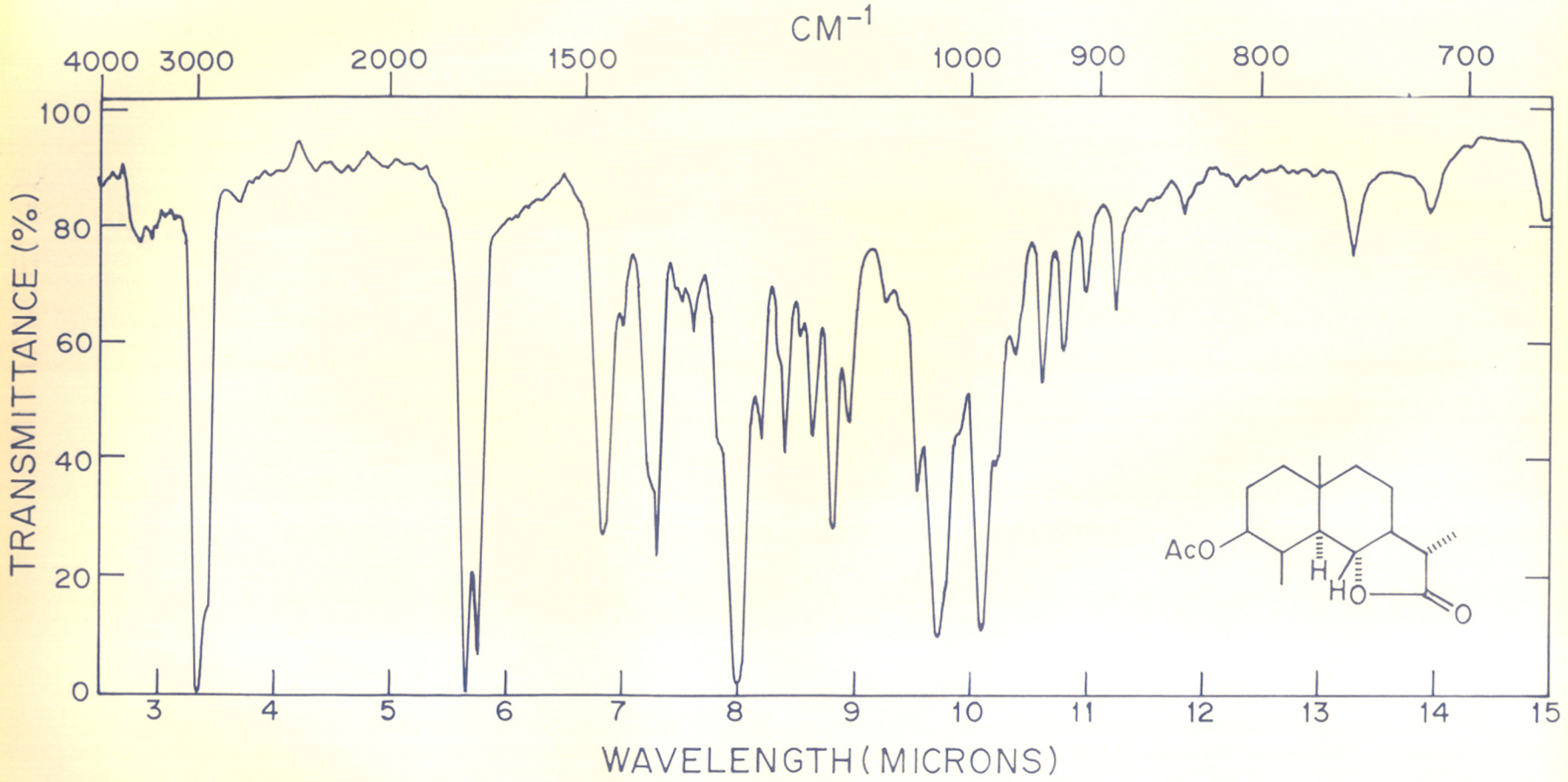
IR SPECTRUM OF 5α(H),6,11β(H)-EUDESM-3-EN-6,13-OLIDE (XX)

(10% SOLUTION IN CS_2, THICKNESS OF THE CELL: 0·2 mm)



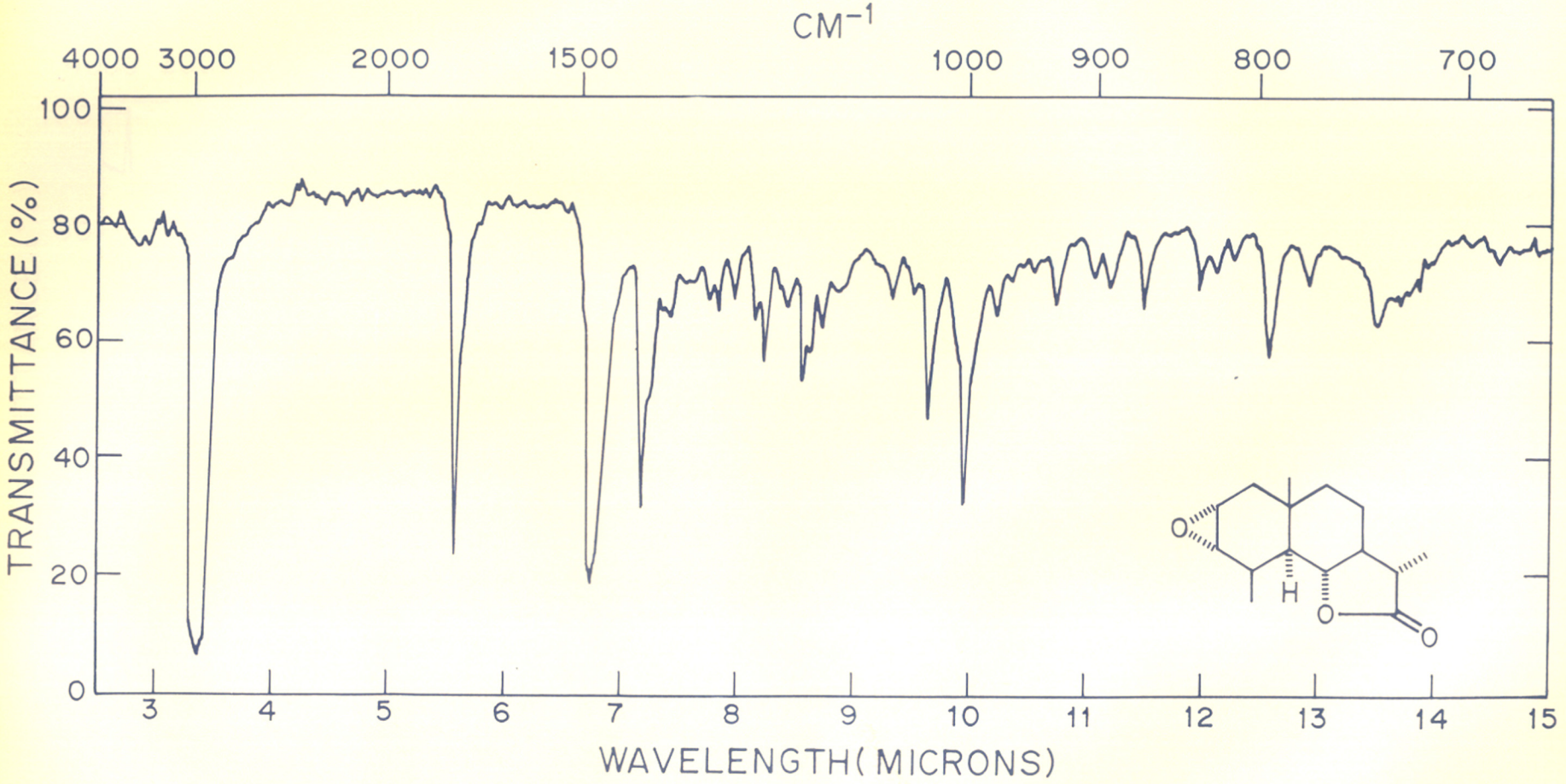
IR SPECTRUM OF 3β-HYDROXY-4,5 α(H),6,11 β(H)-EUDESMAN-6,13-OLIDE (XXIV)

(IN NUJOL)



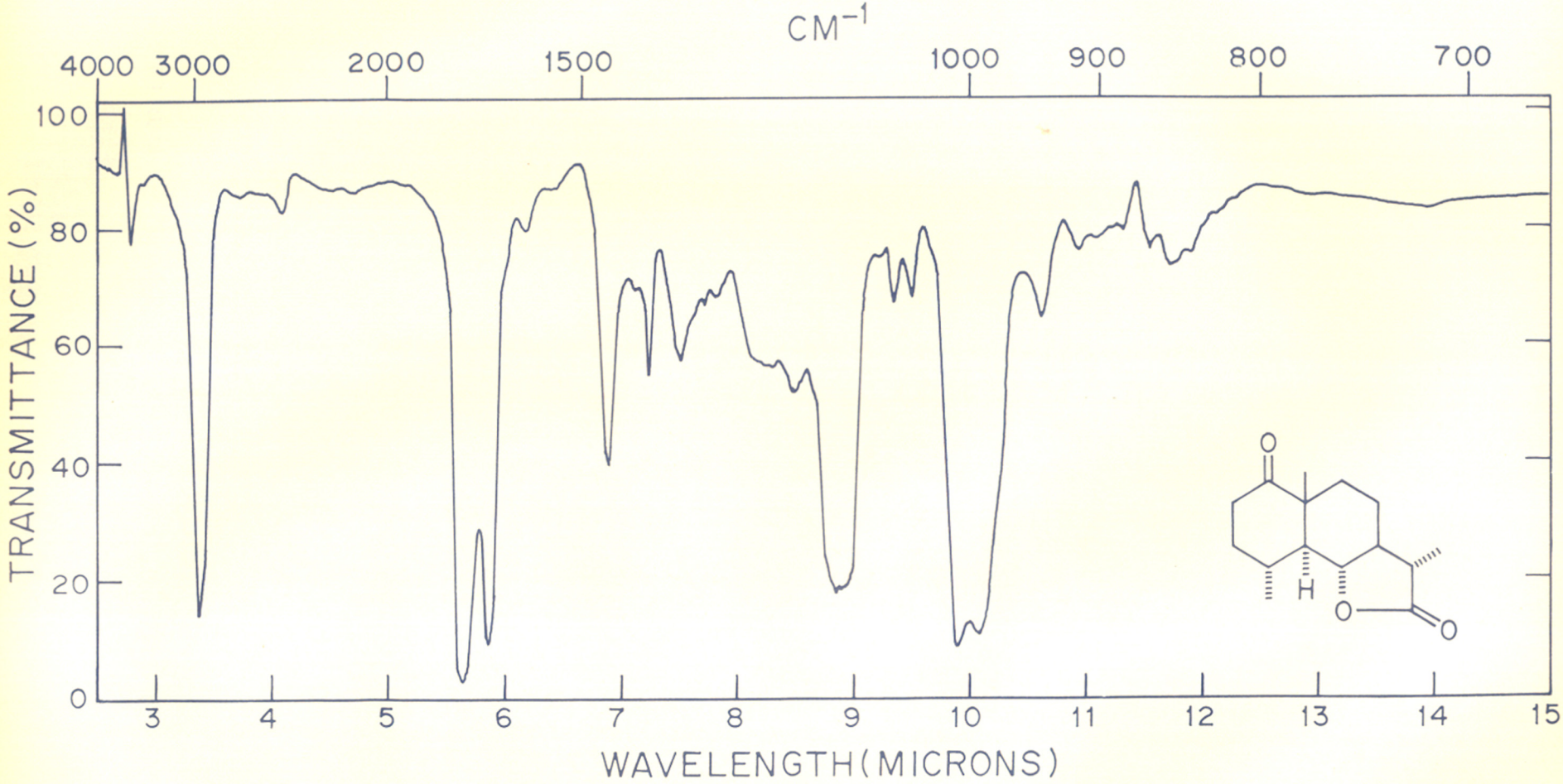
IR SPECTRUM OF 3β-ACETOXY-4,5α(H),6,11β(H)-EUDESMAN-6,13-OLIDE (XXVI)

(IN NUJOL)



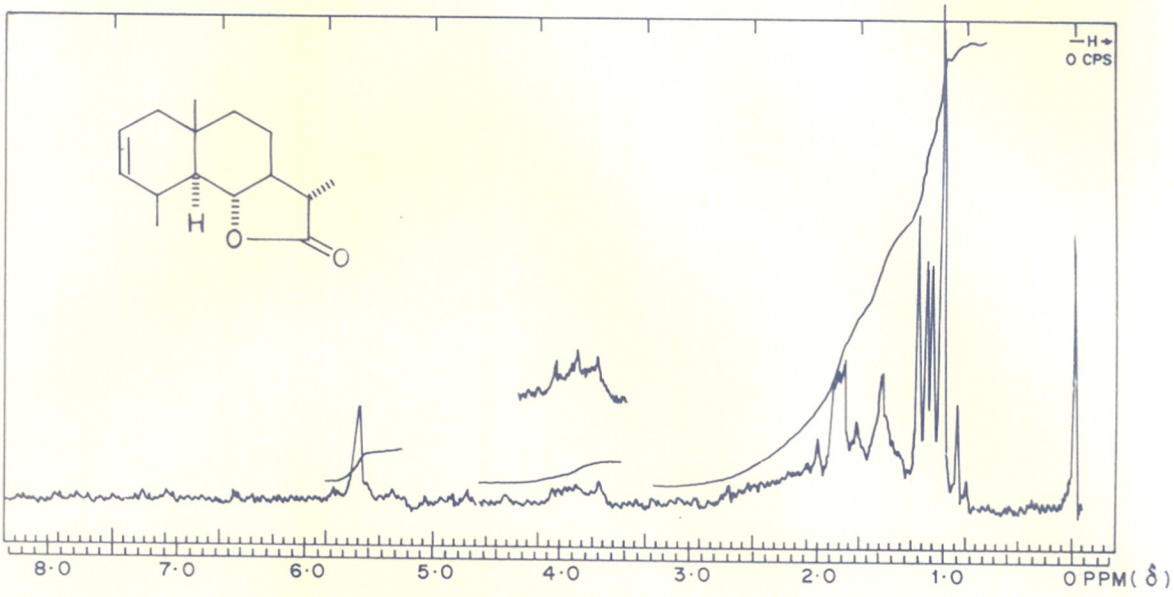
IR SPECTRUM OF 2α,3α-OXIDO-4,5,7α(H),2,3,6,11β(H)-EUDESMAN-6,13-OLIDE (XXXII)

(IN NUJOL)



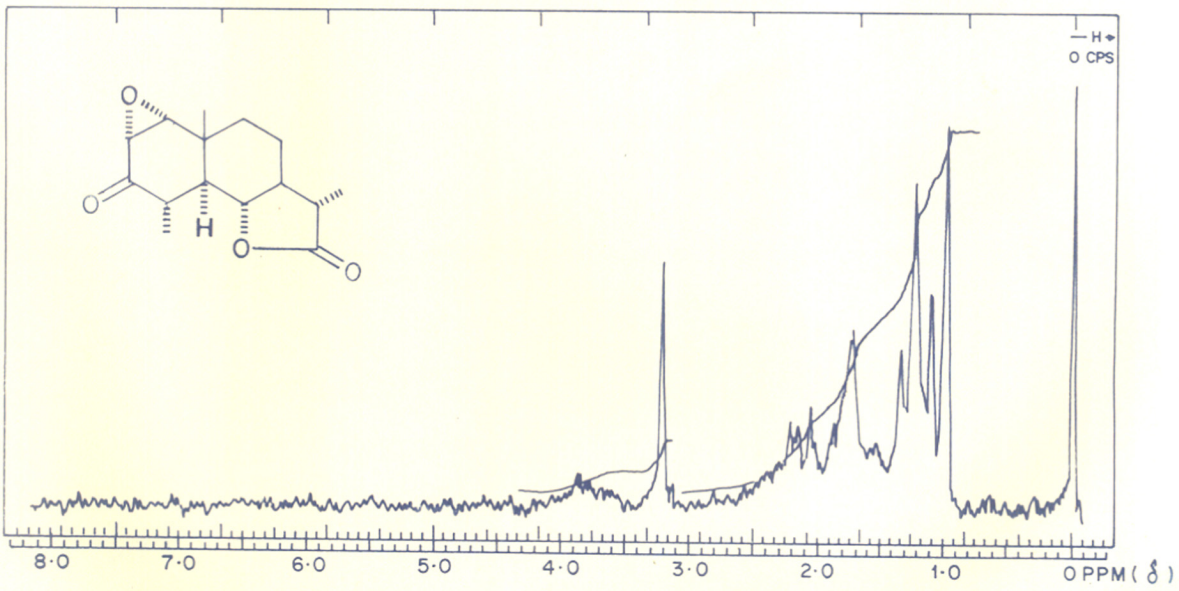
IR SPECTRUM OF 1-OXO-5,7 α (H),4,6,11 β(H)-EUDESMAN-6,13-OLIDE (XXXVI)

(IN $CHCl_3$ SOLUTION)



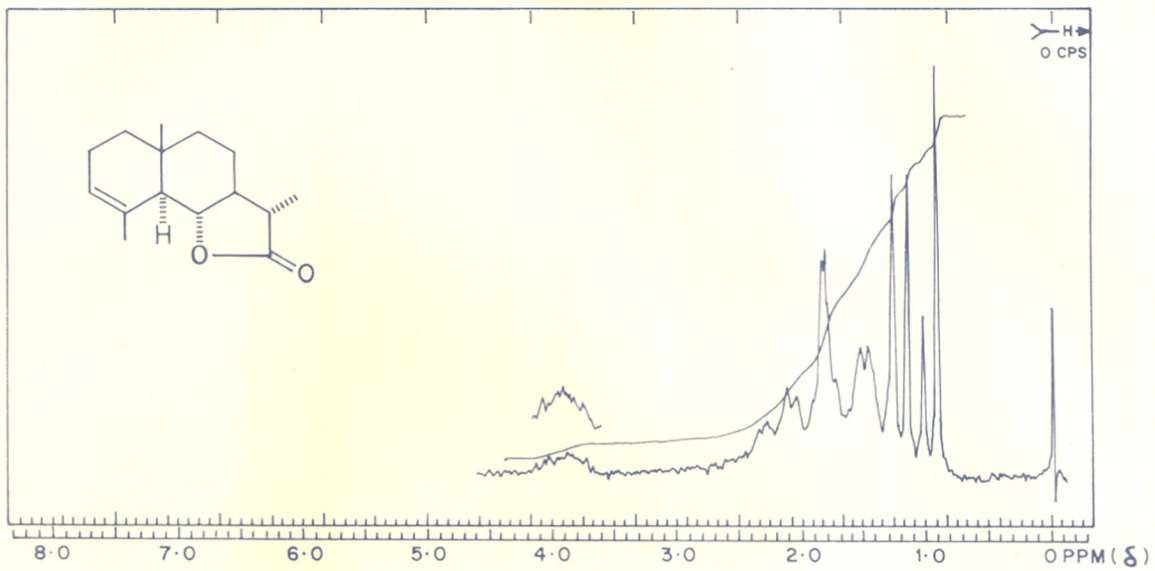
NMR SPECTRUM OF 4,5α(H),6,11β(H)-EUDESM-2-EN-6,13-OLIDE (XIX)

(IN ~~NUJOL~~ CCl_4)



NMR SPECTRUM OF 1α,2α-OXIDO-5,7α(H),1,2,4,6,11β(H)-EUDESMAN-6,13-OLIDE (XV)

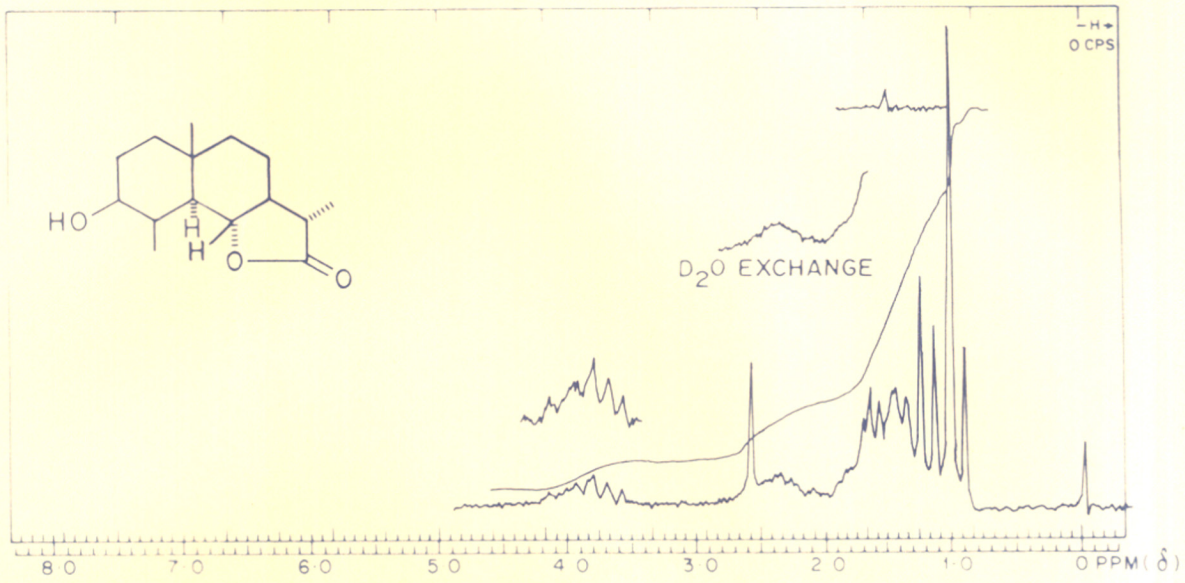
(IN CCl_4)



NMR SPECTRUM OF 5α(H),6,11β(H)-EUDESM-3-EN-6,13-OLIDE (XX)

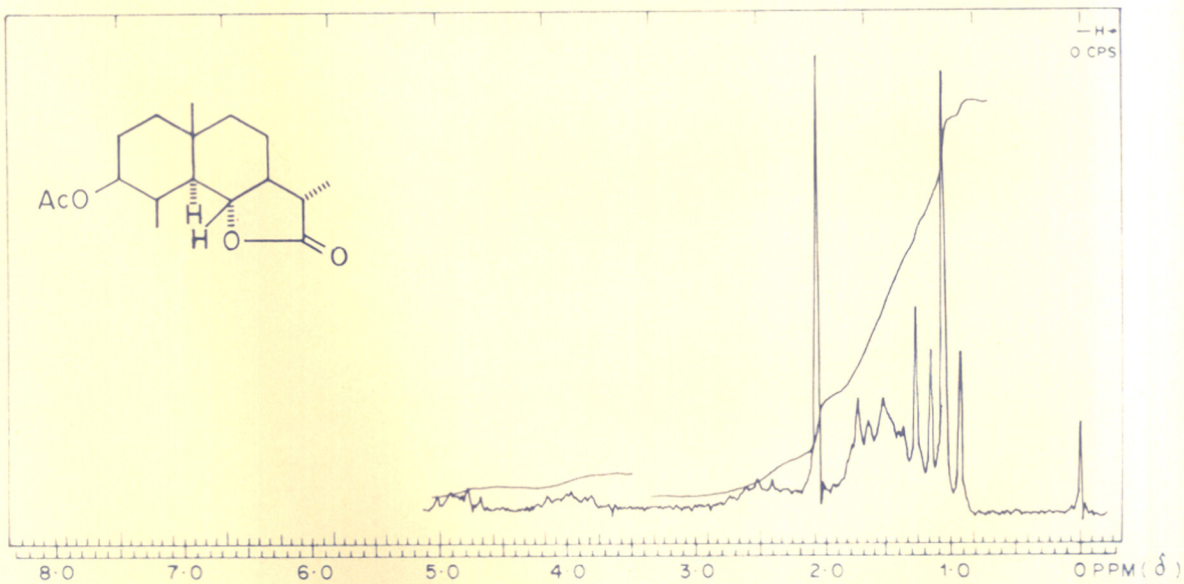
(IN $CHCl_3$)

[PRODUCT OBTAINED BY ACTION OF KtBD REAGENT ON TOSYLATE OF (XXIV) - PROBABLY CONTAMINATED WITH Δ^2-SANTENOLIDE]



NMR SPECTRUM OF 3β-HYDROXY-4,5α(H),6,11β(H)-EUDESMAN-6,13-OLIDE (XXIV)

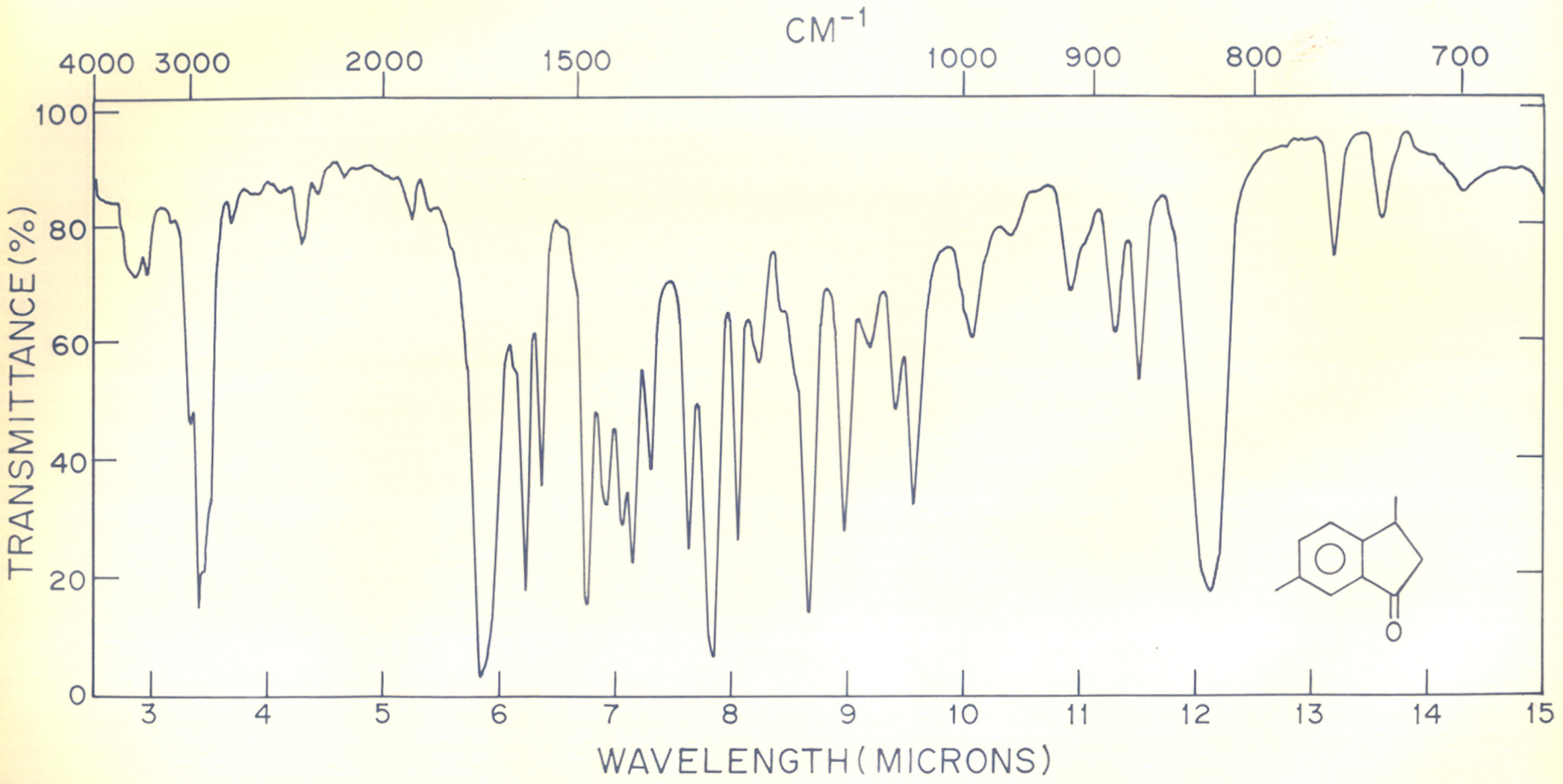
(IN $CHCl_3$)



NMR SPECTRUM OF 3β-ACETOXY-4,5α(H),6,11β(H)-EUDESMAN-6,13-OLIDE (XXVI)

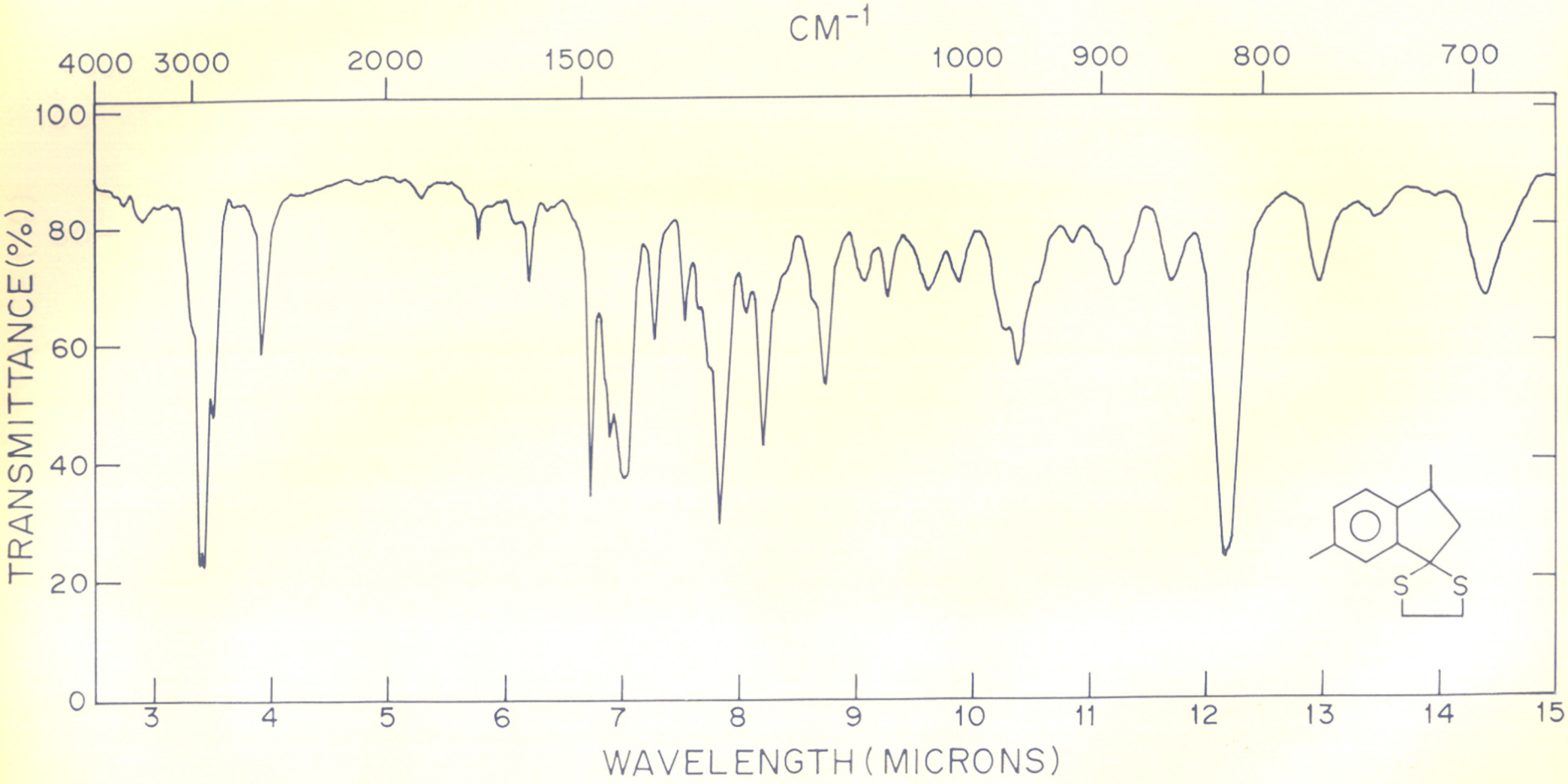
(IN $CHCl_3$)

CHAPTER II



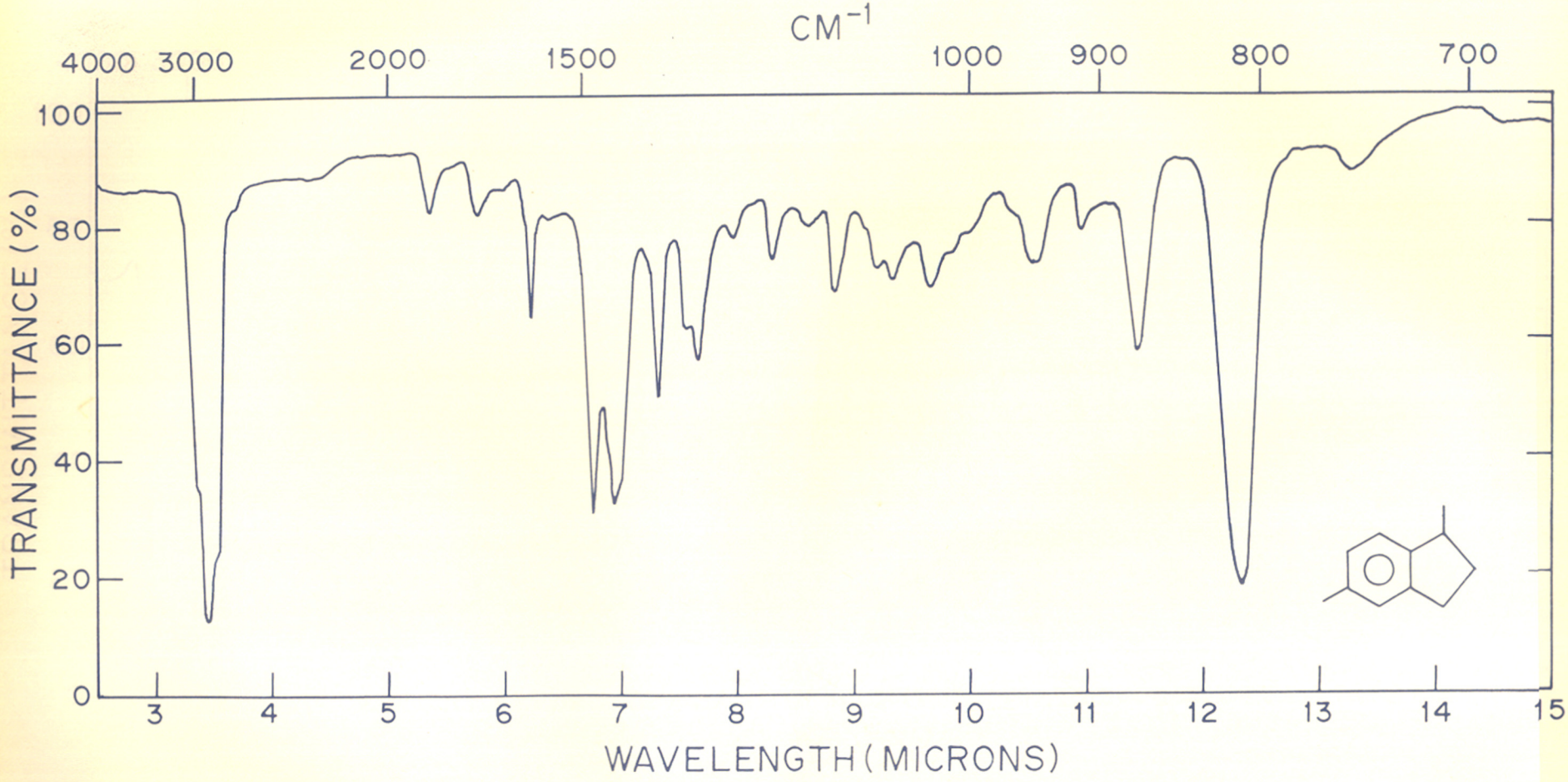
IR SPECTRUM OF 3,6-DIMETHYLINDANE-1-ONE (VII)

(LIQ.FILM)



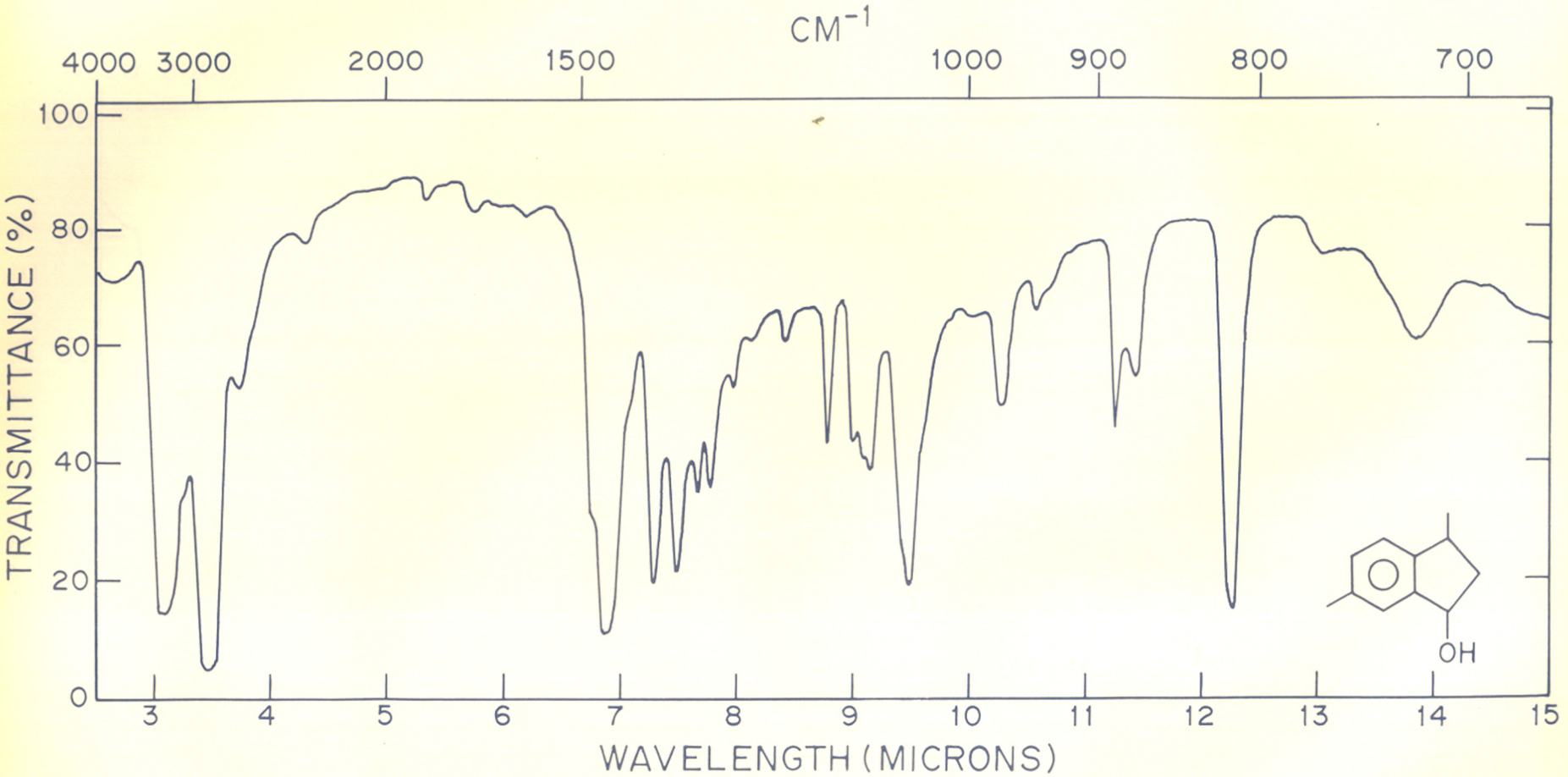
IR SPECTRUM OF 1-ETHYLENEDITHIO-3,6-DIMETHYLINDANE (VIII)

(LIQ. FILM)



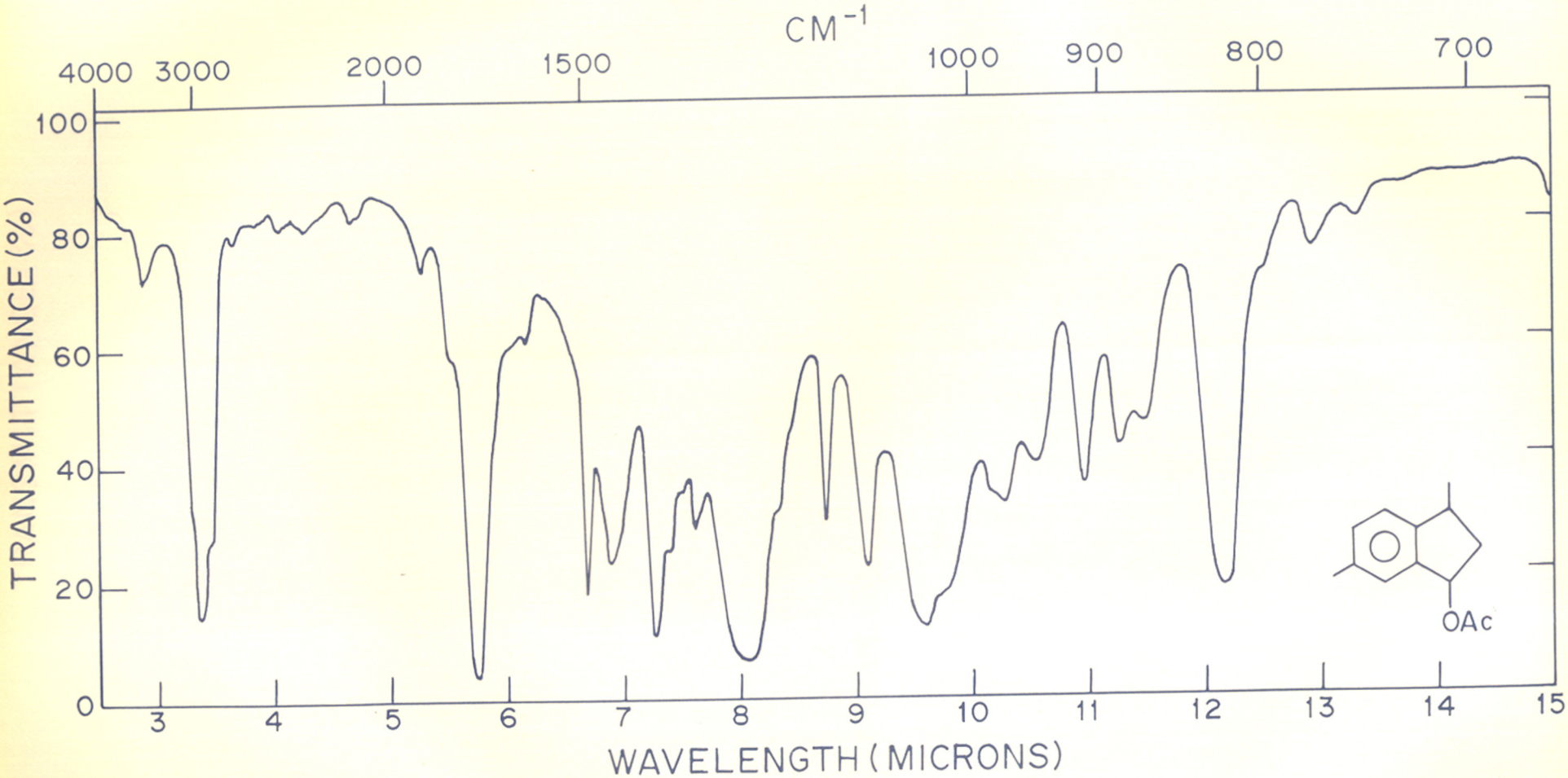
IR SPECTRUM OF 1,5-DIMETHYLINDANE (IX)

(LIQ·FILM)



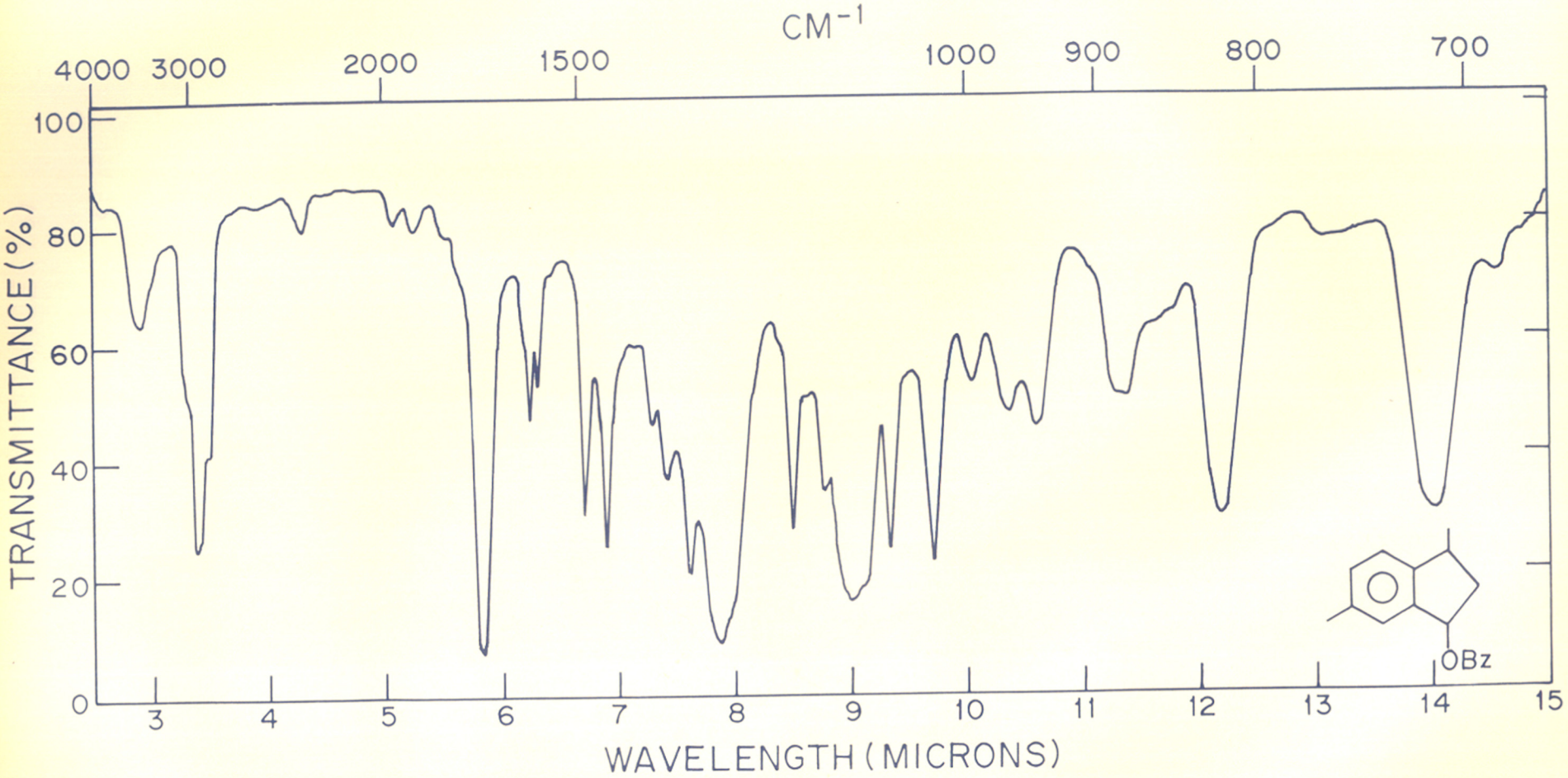
IR SPECTRUM OF 3β,6-DIMETHYLINDANE-1β-OL (X)

(IN NUJOL)



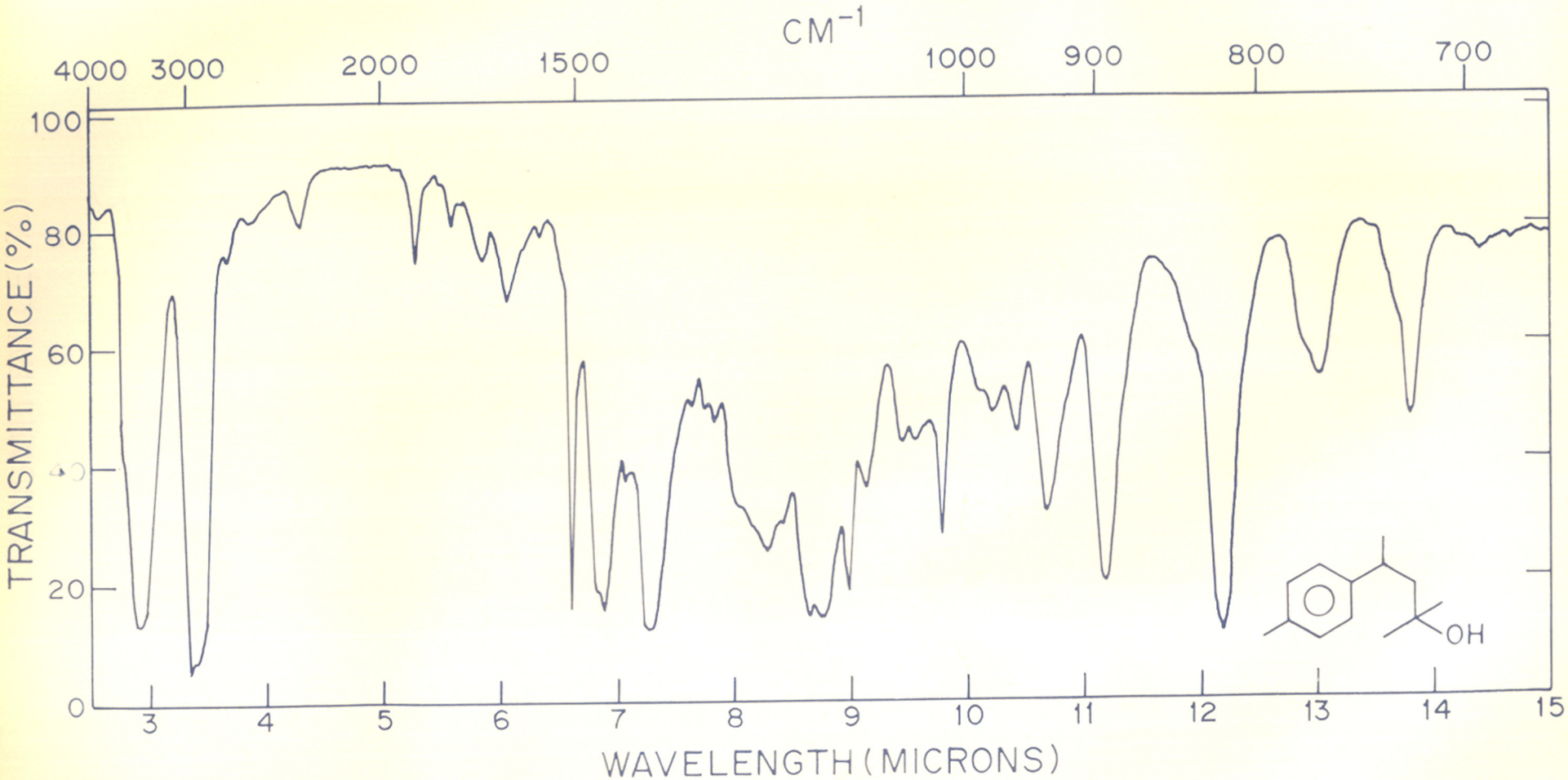
IR SPECTRUM OF 3β, 6-DIMETHYL-1β-ACETOXYINDANE (XIV)

(LIQ. FILM)



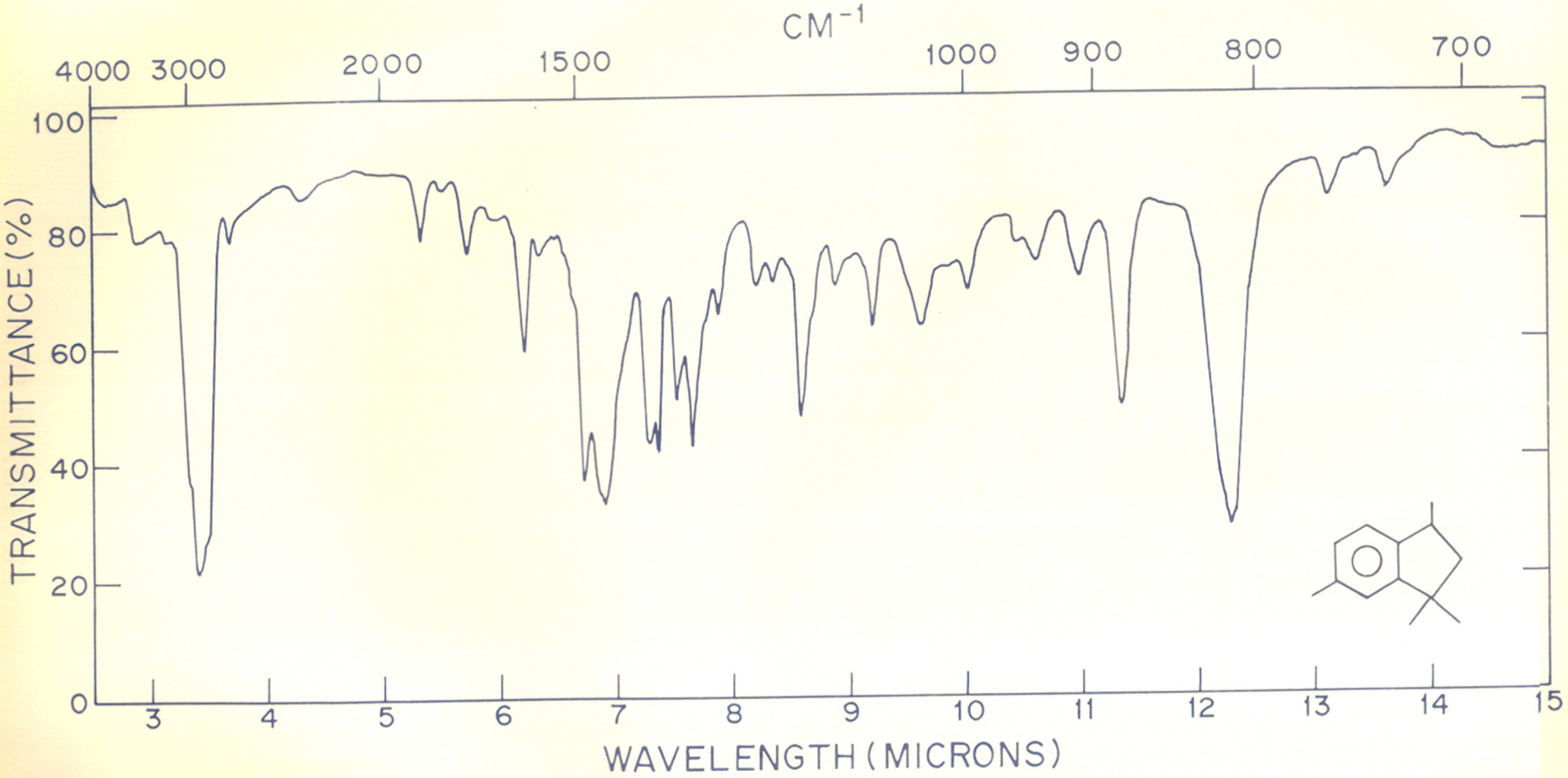
IR SPECTRUM OF 3β, 6-DIMETHYL-1β-BENZOYLOXYINDANE (XV)

(LIQ. FILM)



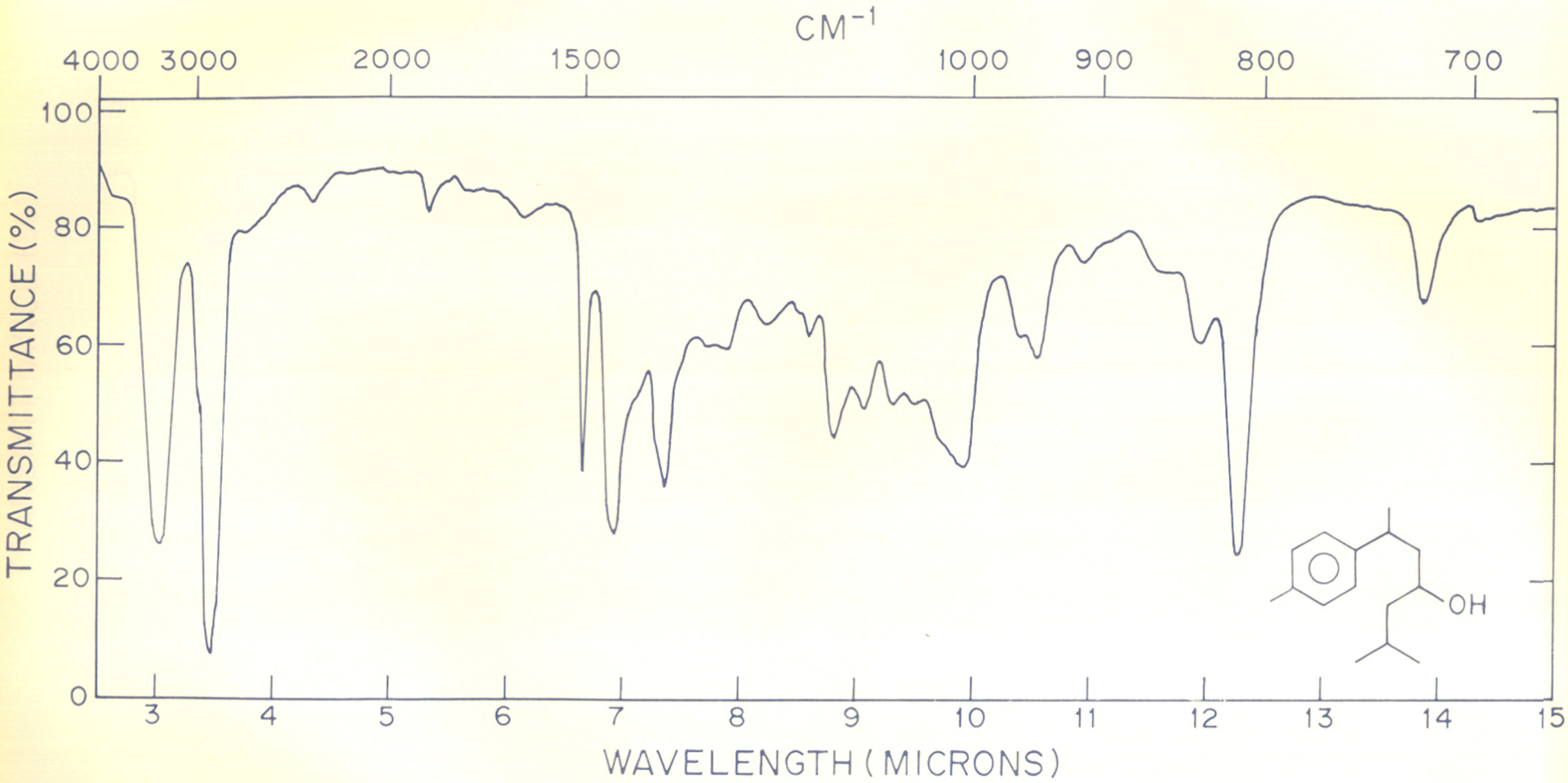
IR SPECTRUM OF 2-METHYL-4-p-TOLYLPENTANE-2-OL (XVI)

(LIQ. FILM)



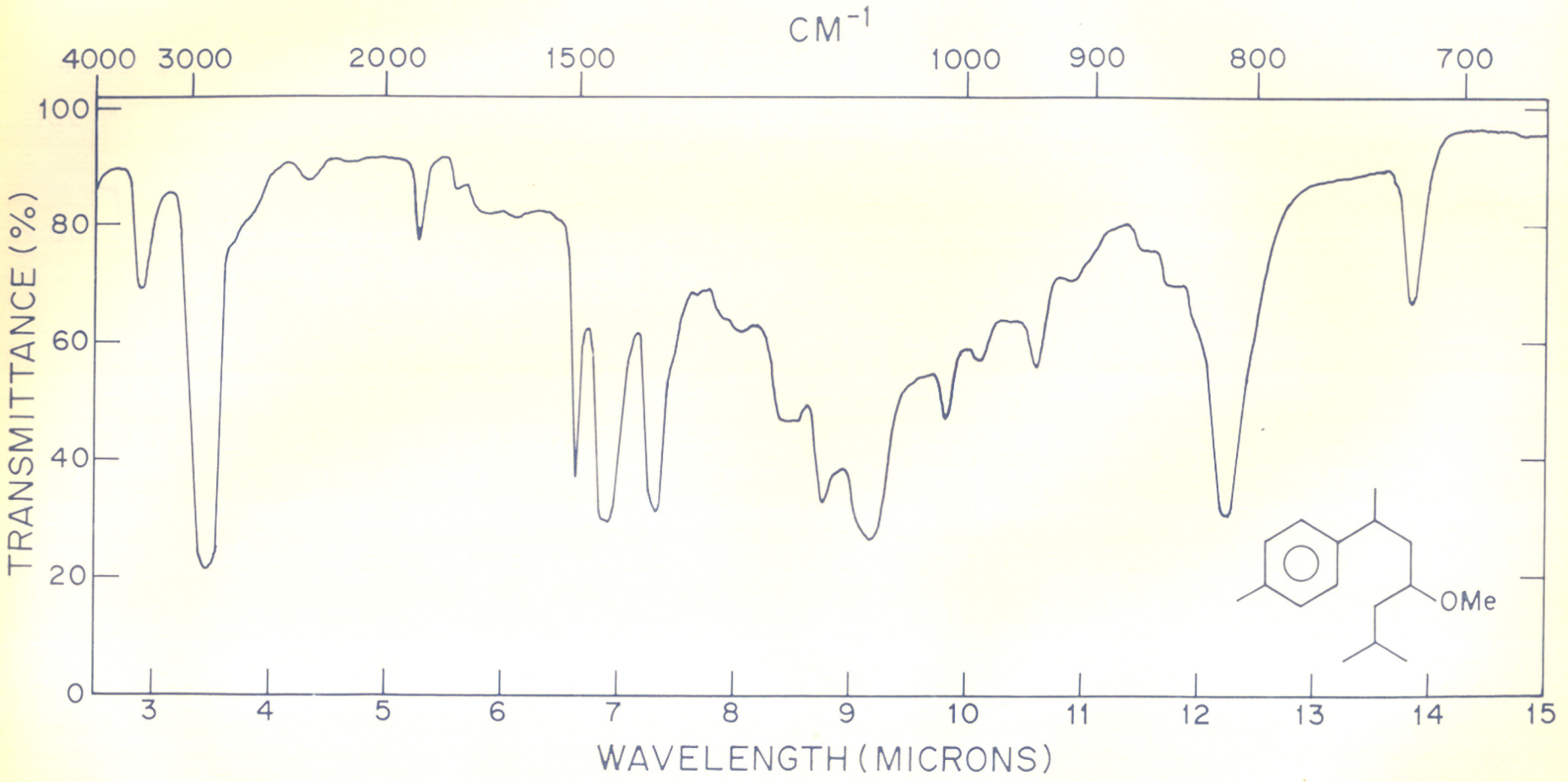
IR SPECTRUM OF 1,1,3,6-TETRAMETHYLINDANE (XVIII)

(LIQ. FILM)



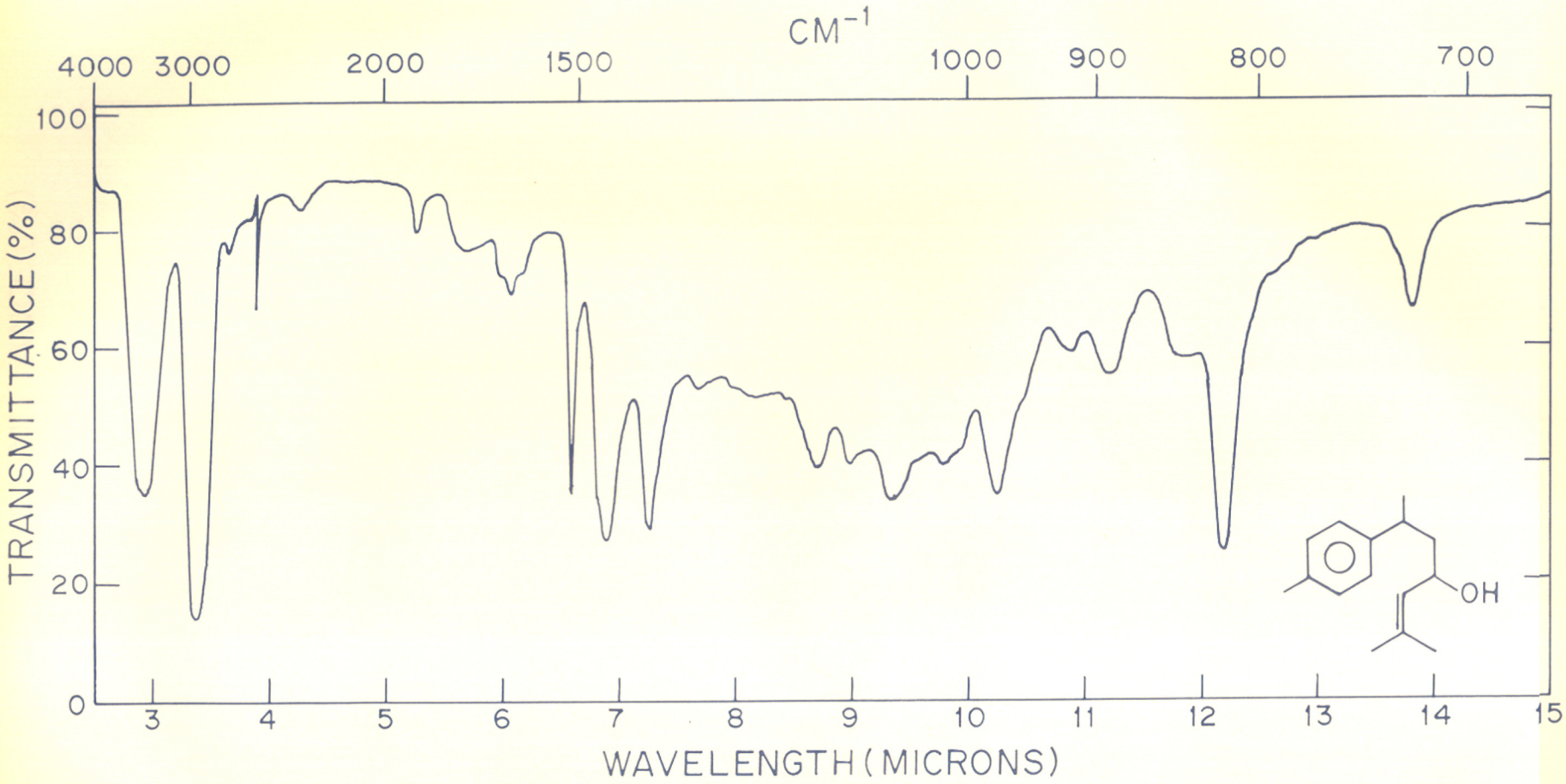
IR SPECTRUM OF 2-METHYL-6-p-TOLYLHEPTANE-4-OL (XX)

(LIQ. FILM)



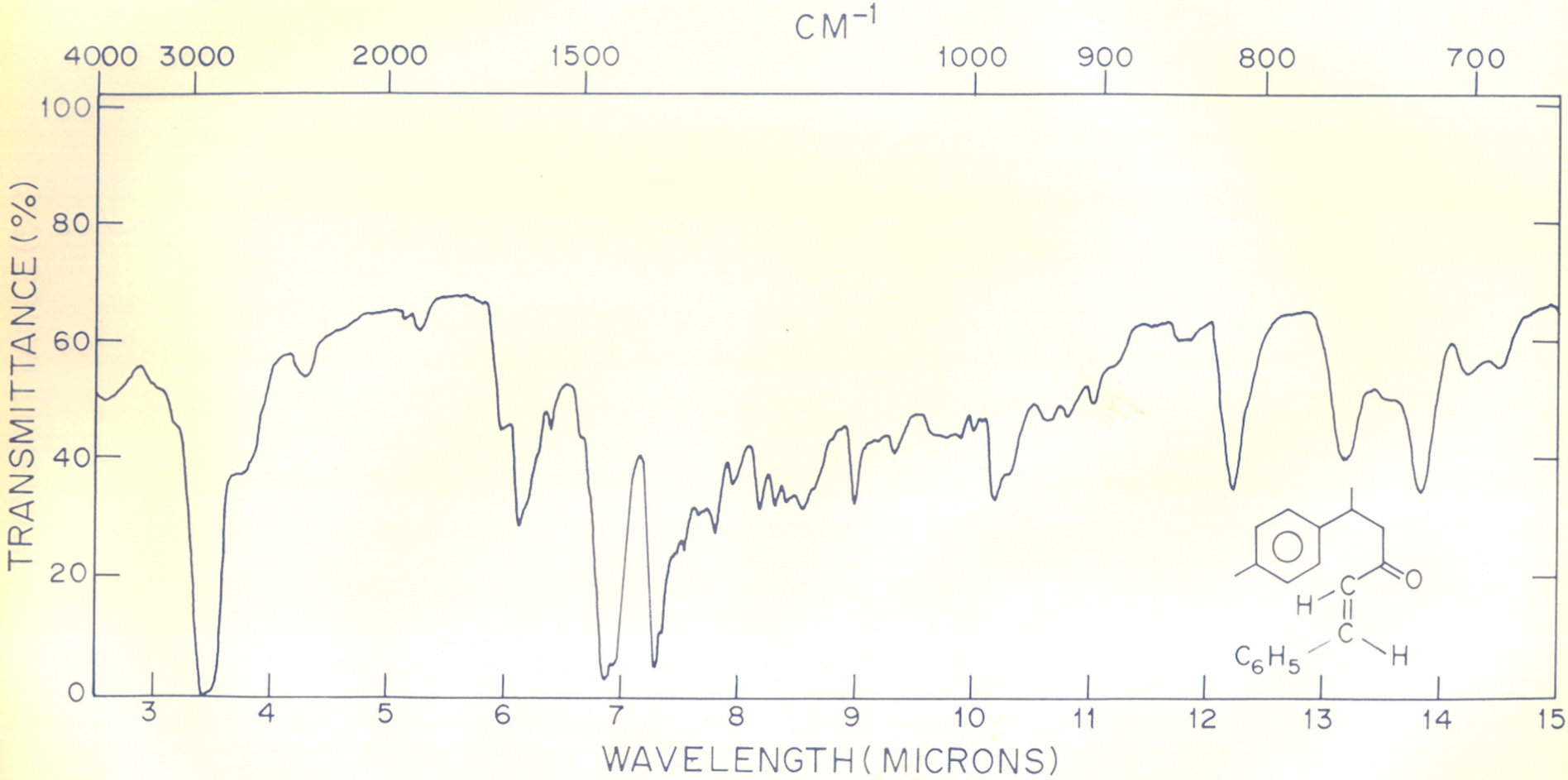
IR SPECTRUM OF 2-METHYL-4-METHOXY-6-p-TOLYLHEPTANE (XXI)

(LIQ FILM)



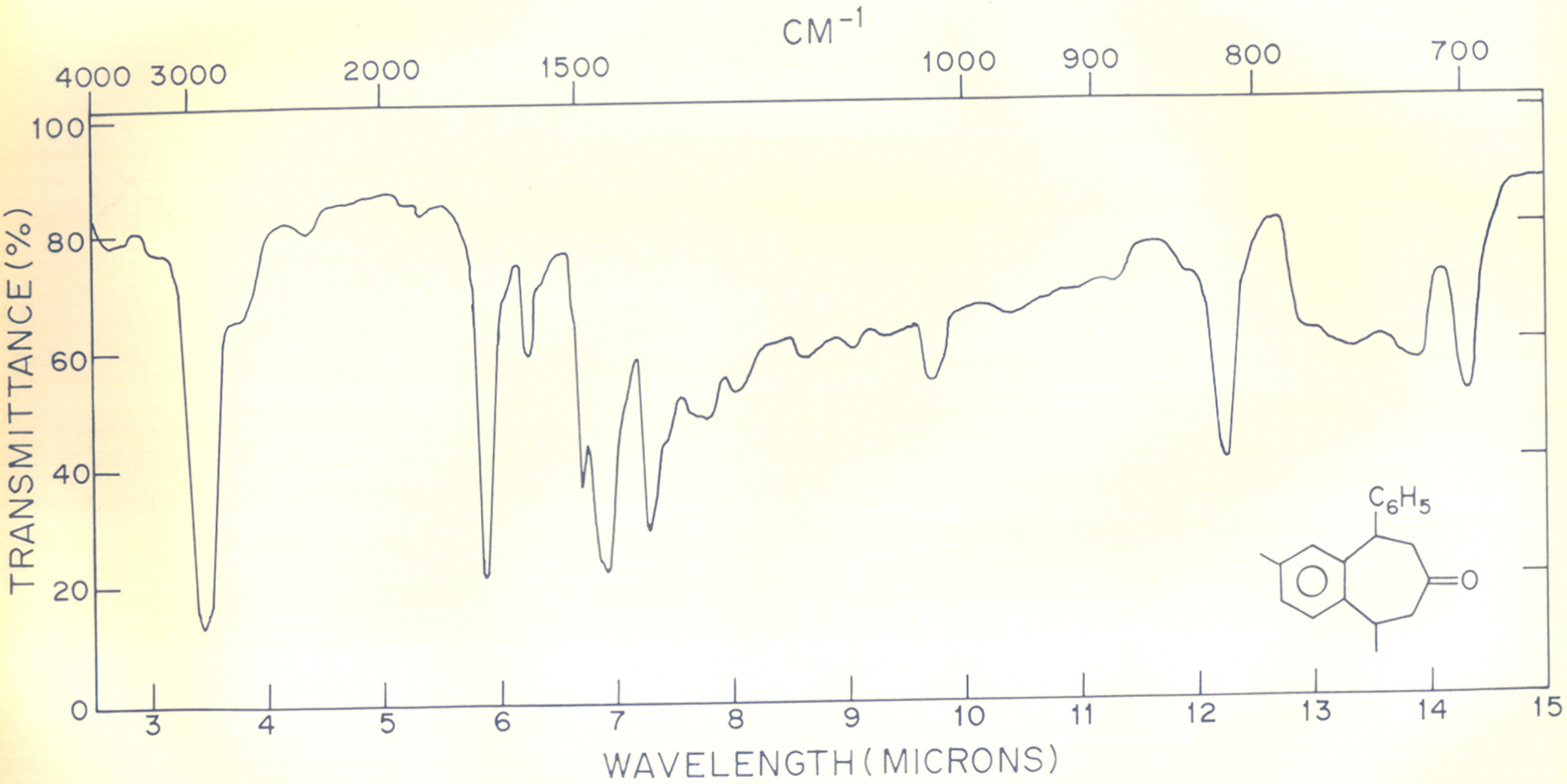
IR SPECTRUM OF 2-METHYL-6-p-TOLYLHEPT-2-ENE-4-OL (XXV)

(LIQ. FILM)



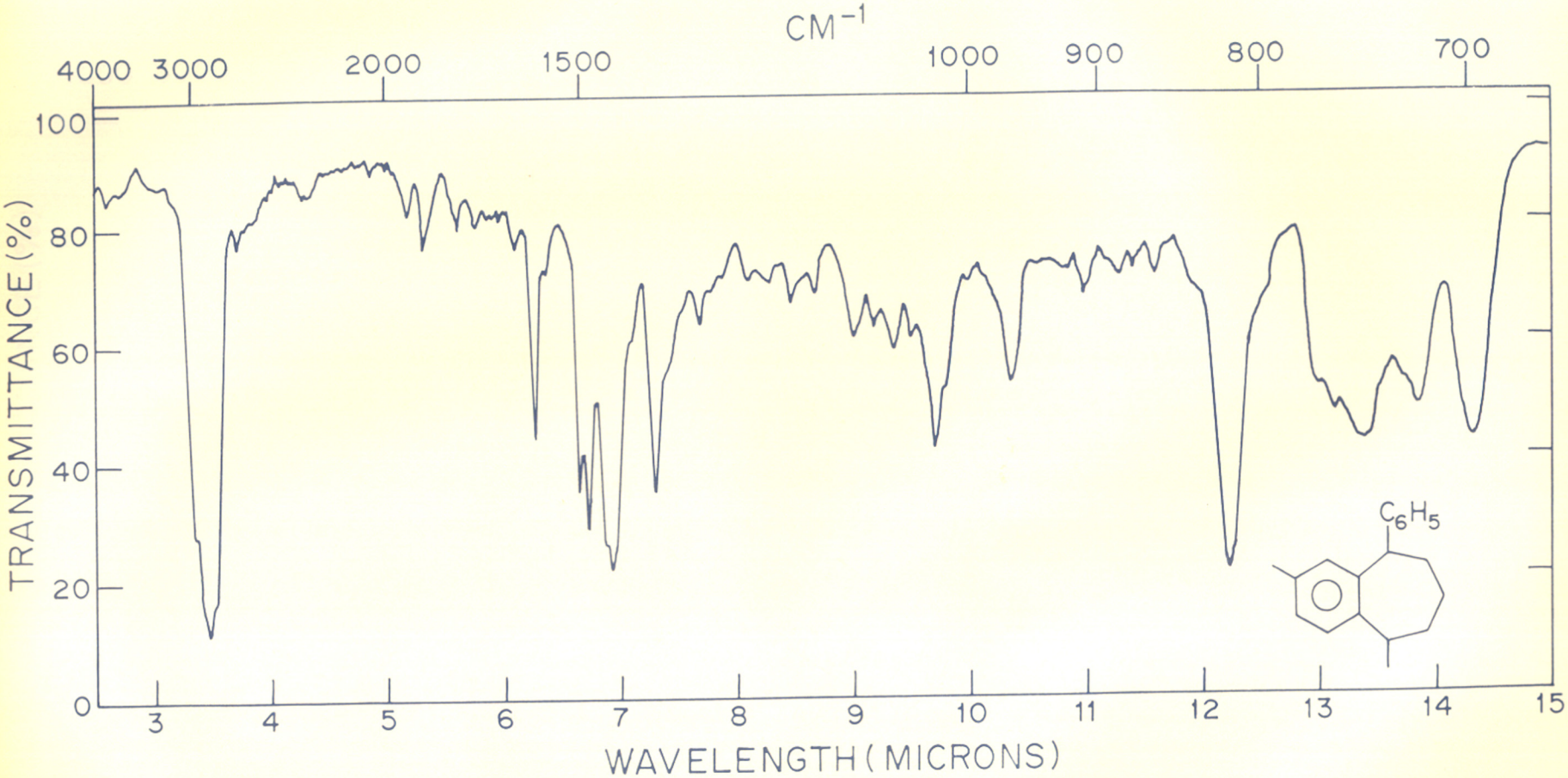
IR SPECTRUM OF 1-PHENYL-5-p-TOLYLHEX-1-ENE-3-ONE (XXXI)

(IN NUJOL)



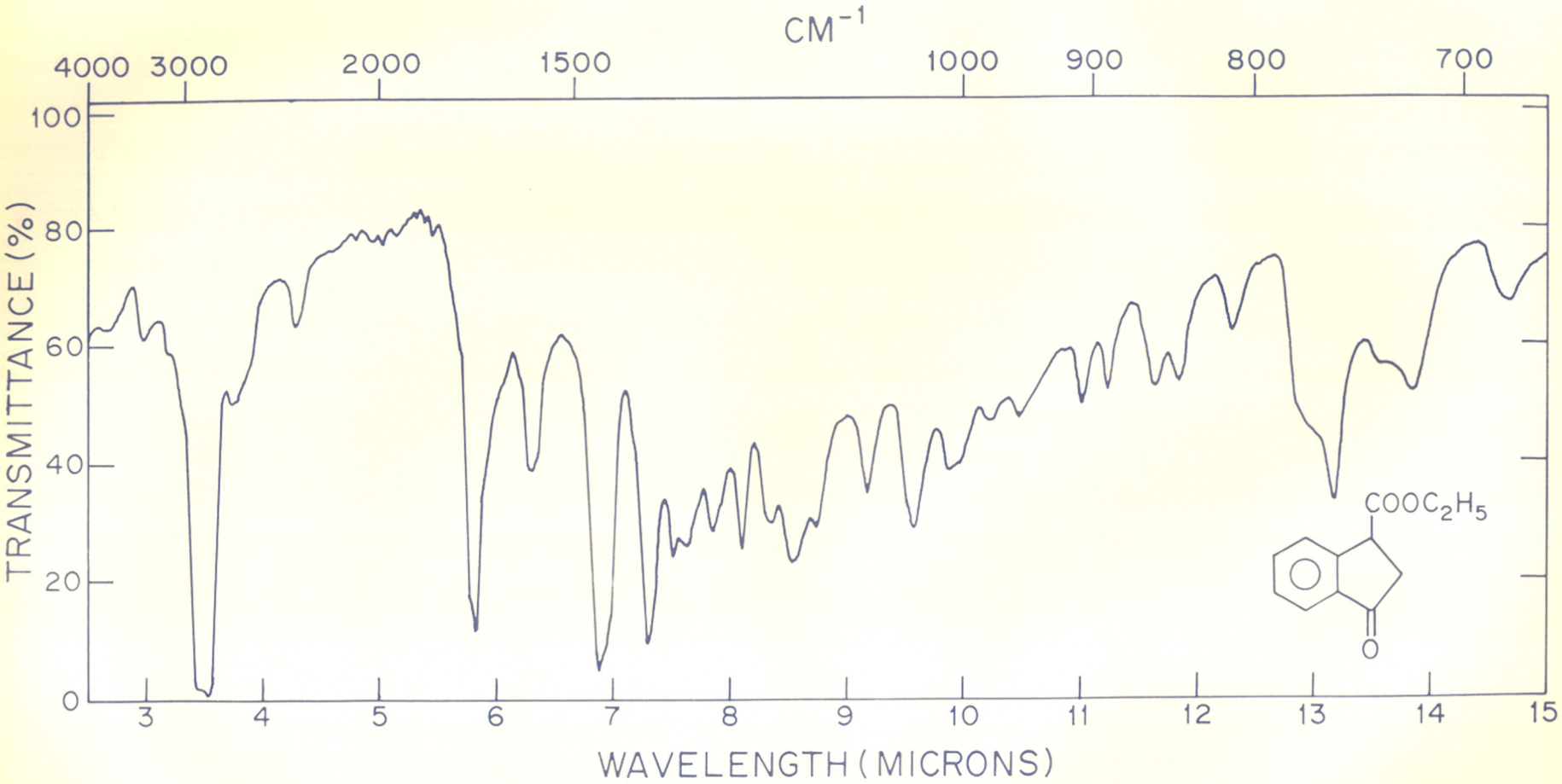
IR SPECTRUM OF 2,5-DIMETHYL-9-PHENYL-7-OXO-BENZOSUBERANE (XXXII)

(IN NUJOL)



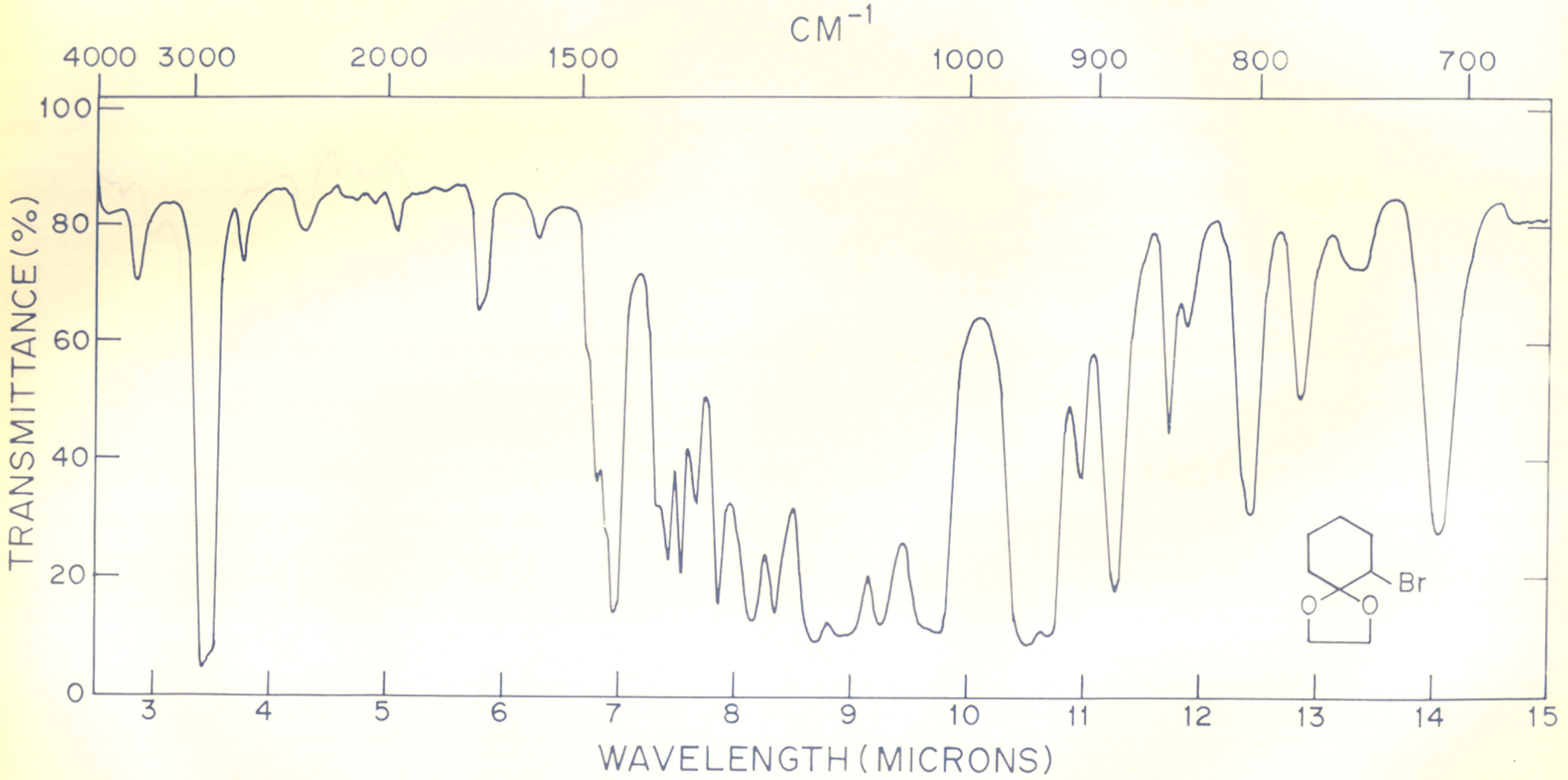
IR SPECTRUM OF 2,5-DIMETHYL-9-PHENYLBENZOSUBERANE (XXXIV)

(TRACE OF NUJOL)



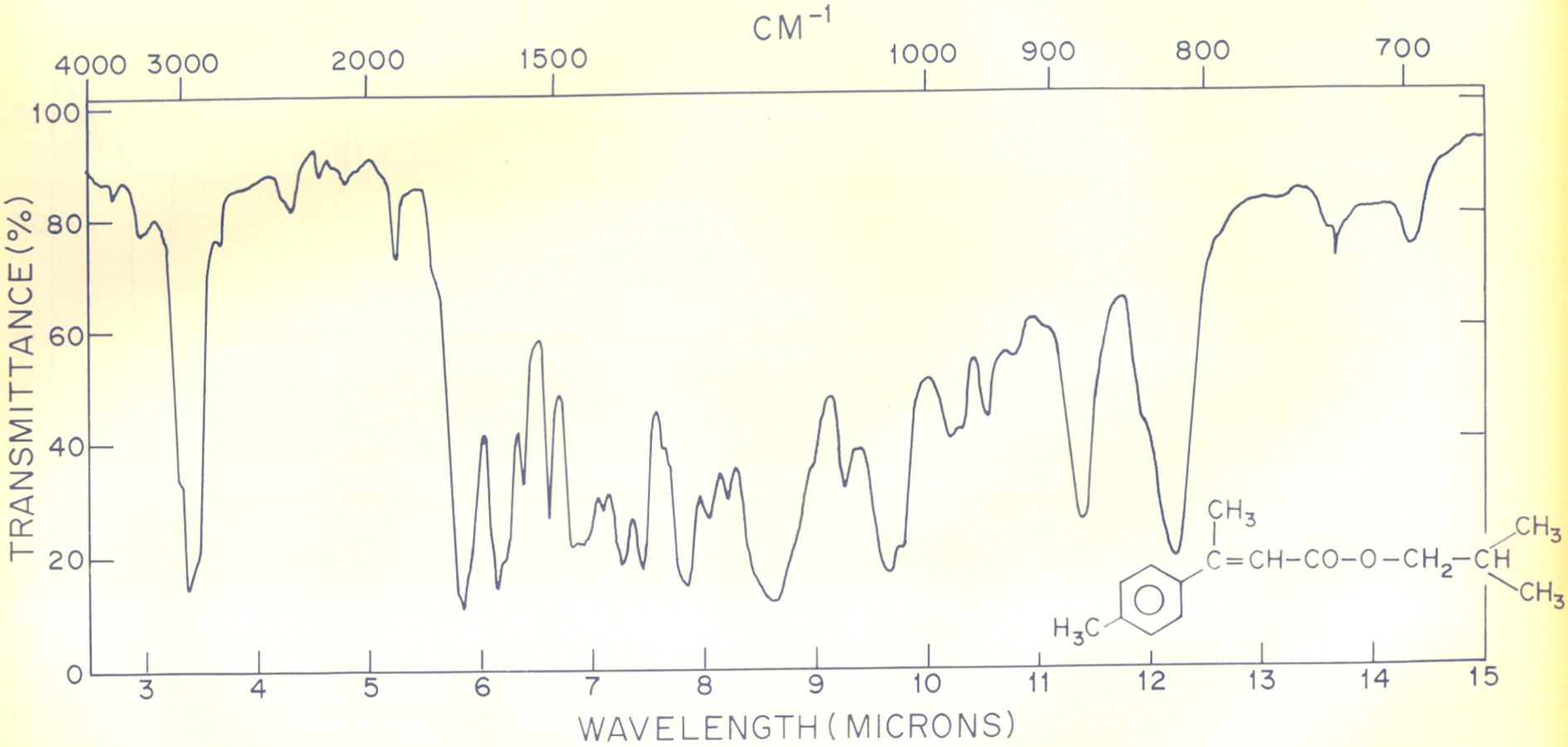
IR SPECTRUM OF ETHYL ESTER OF 1-OXO-INDANE-3-CARBOXYLIC ACID (XXXVIII)

(IN NUJOL)



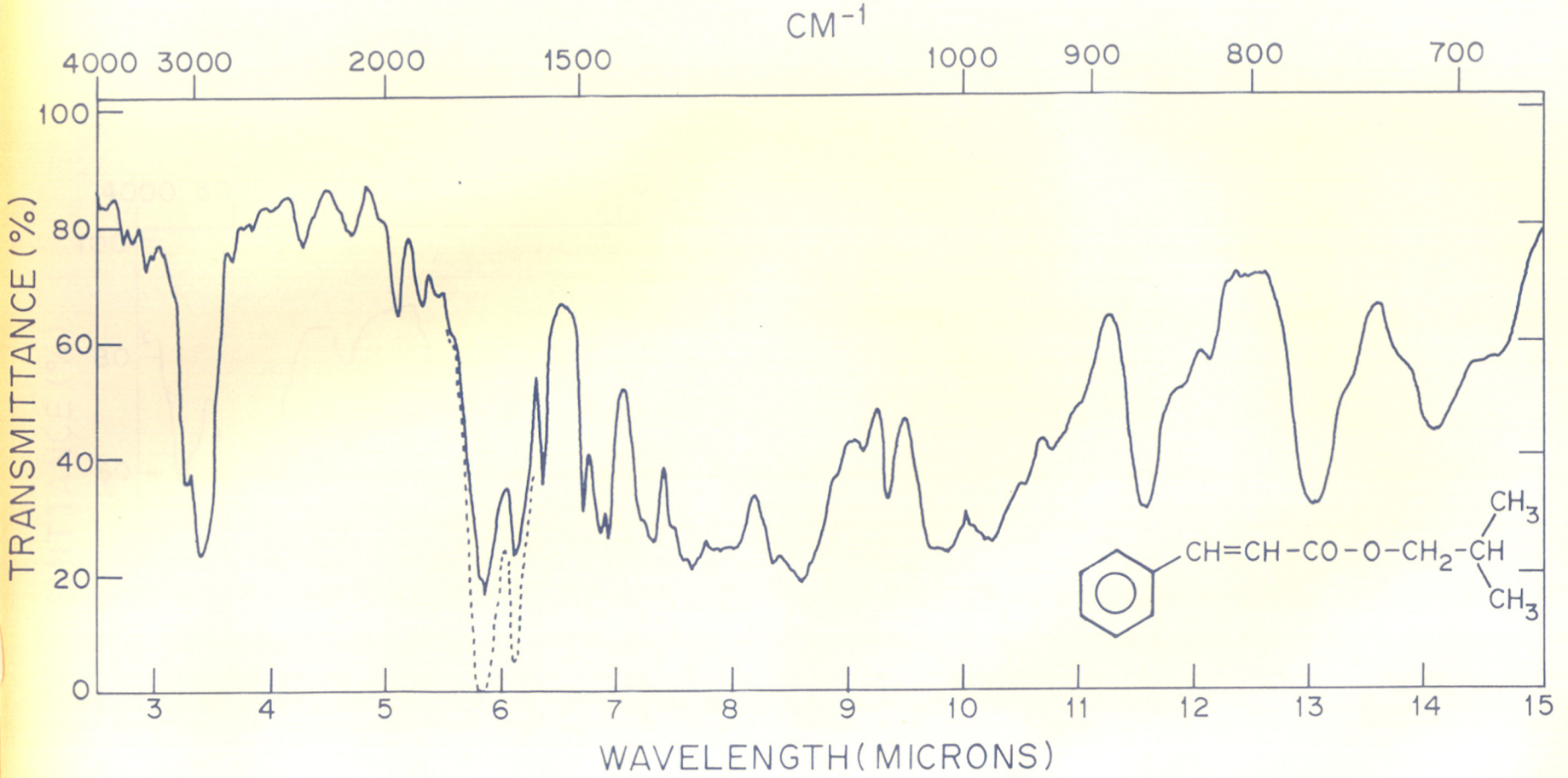
IR SPECTRUM OF 1-ETHYLENEDIOXY-2-BROMOCYCLOHEXANE (XLIII)

(LIQ. FILM)



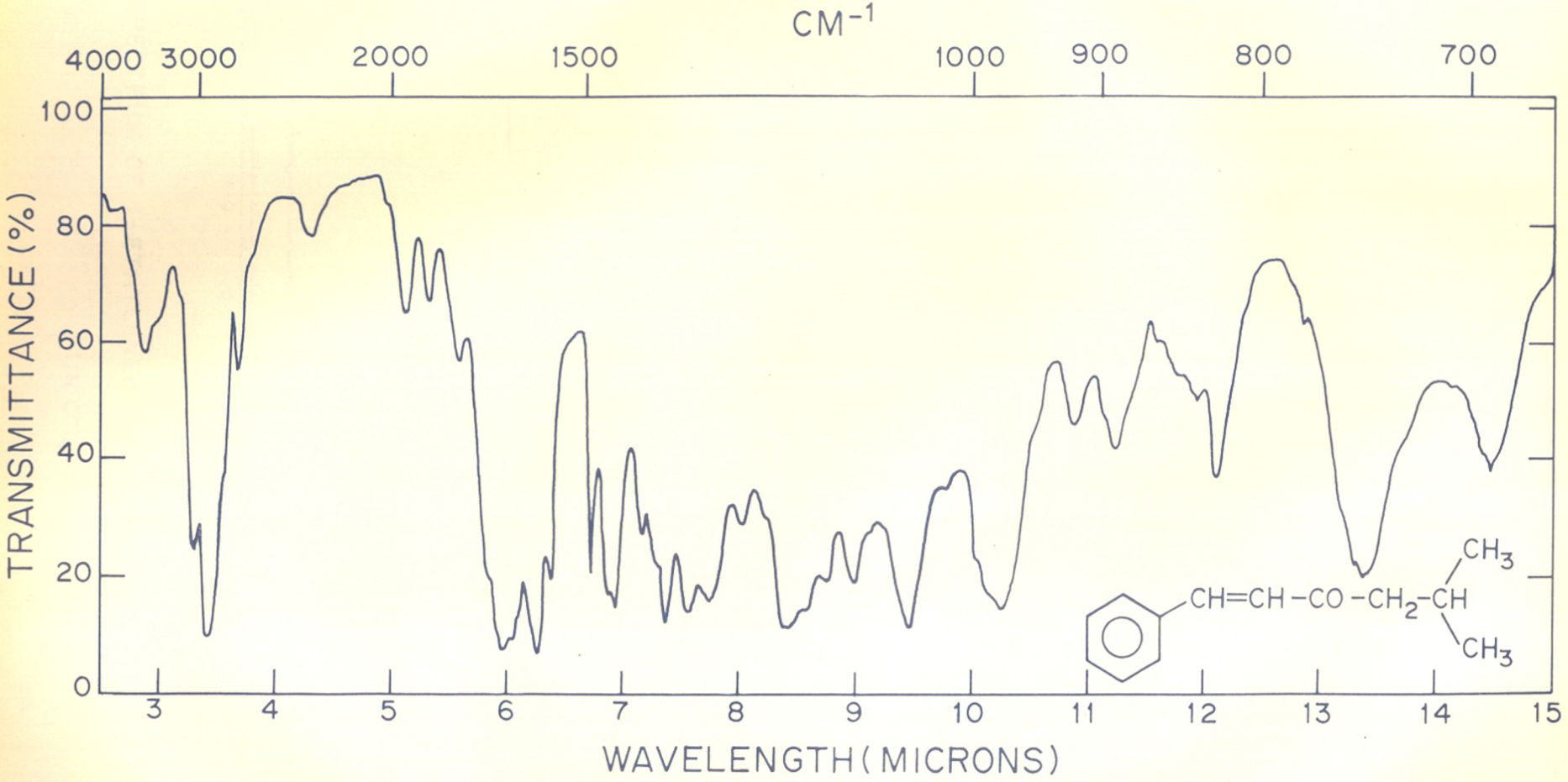
IR SPECTRUM OF ISOBUTYL ESTER OF 3-p-TOLYLBUT-2-ENOIC ACID (LIX)

(LIQ. FILM)



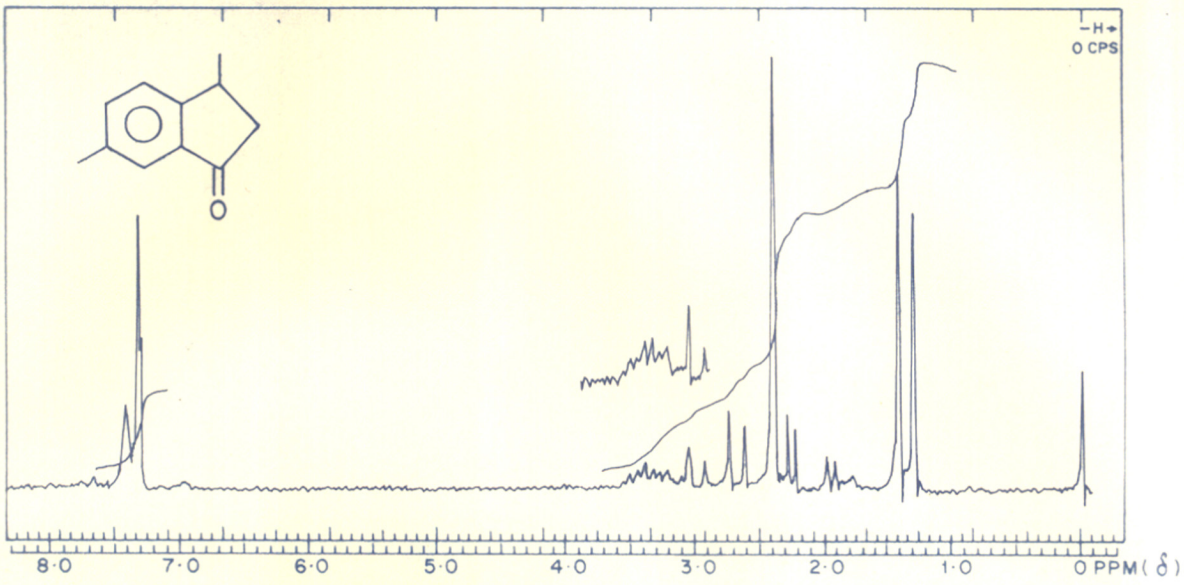
IR SPECTRUM OF ISOBUTYL ESTER OF 3-PHENYLPROP-2-ENOIC ACID (LXII)

—— LIQ·FILM ; ---- THICKER FILM



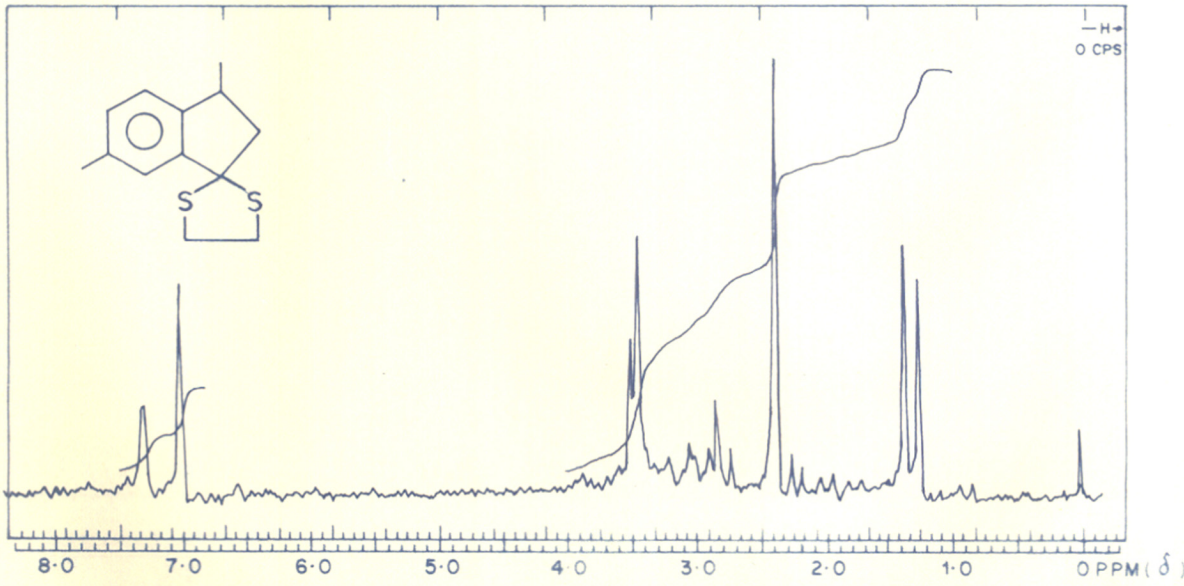
IR SPECTRUM OF 2-METHYL-6-PHENYLHEX-5-EN-4-ONE (LXV)

(LIQ. FILM)



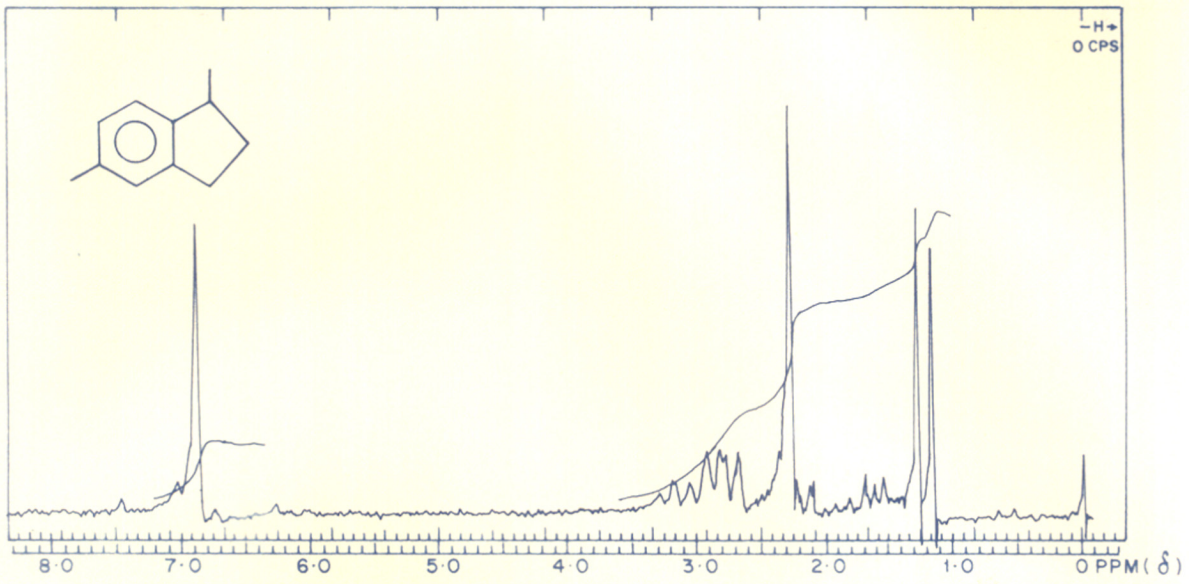
NMR SPECTRUM OF 3,6-DIMETHYLINDANE-1-ONE (VII)

(IN CCl_4)



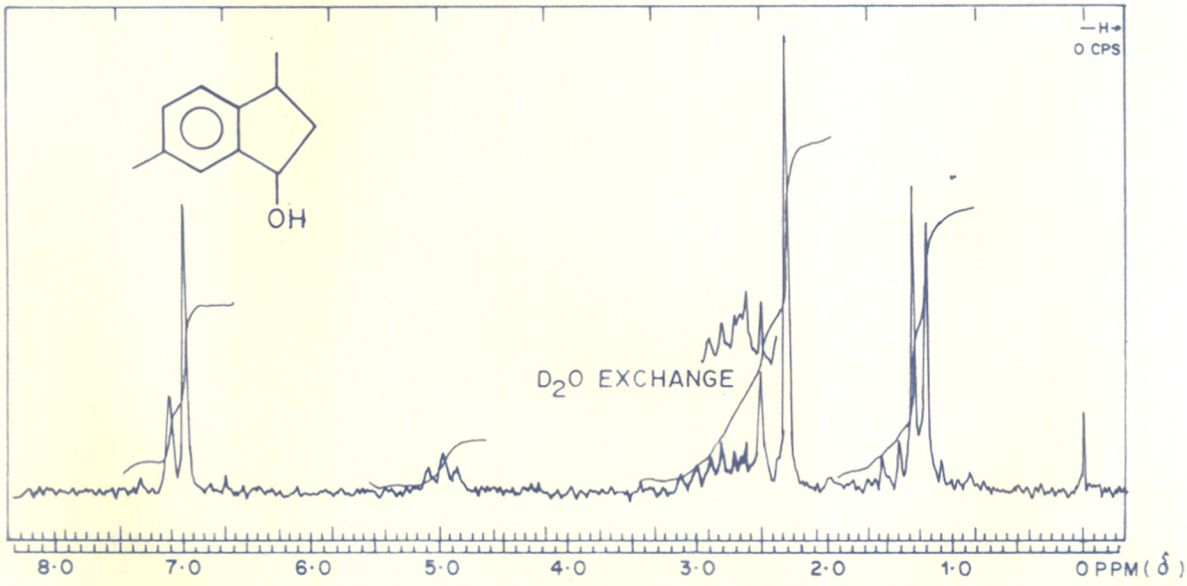
NMR SPECTRUM OF 1-ETHYLENEDITHIO-3,6-DIMETHYLINDANE (VIII)

(IN CCl_4)



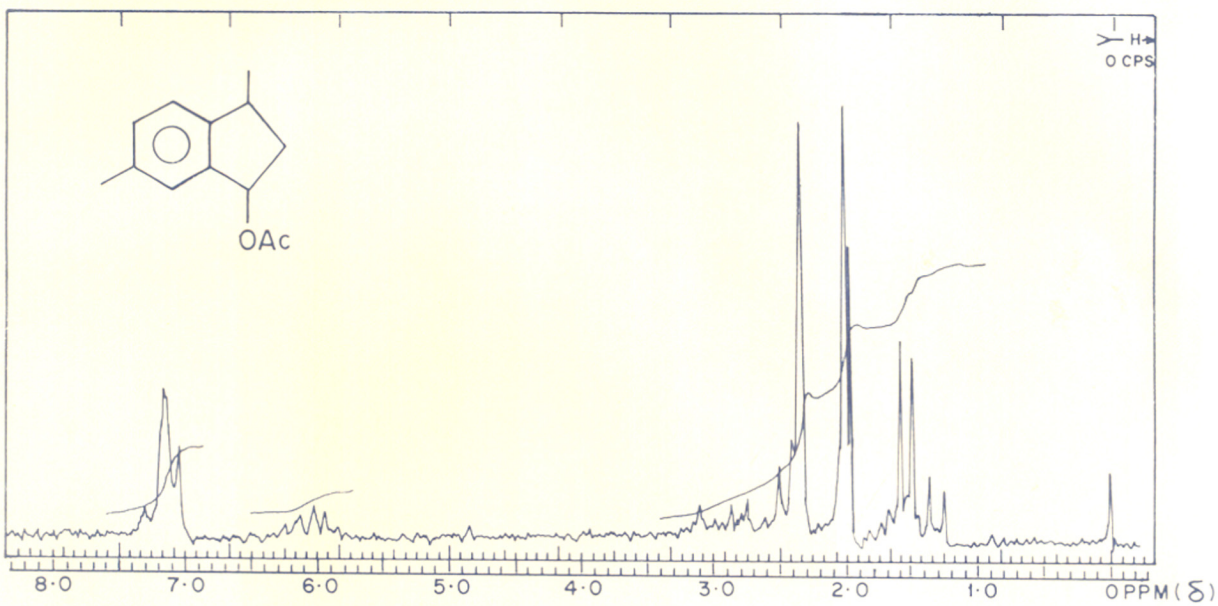
NMR SPECTRUM OF 1,5-DIMETHYLINDANE (IX)

(IN CCl_4)



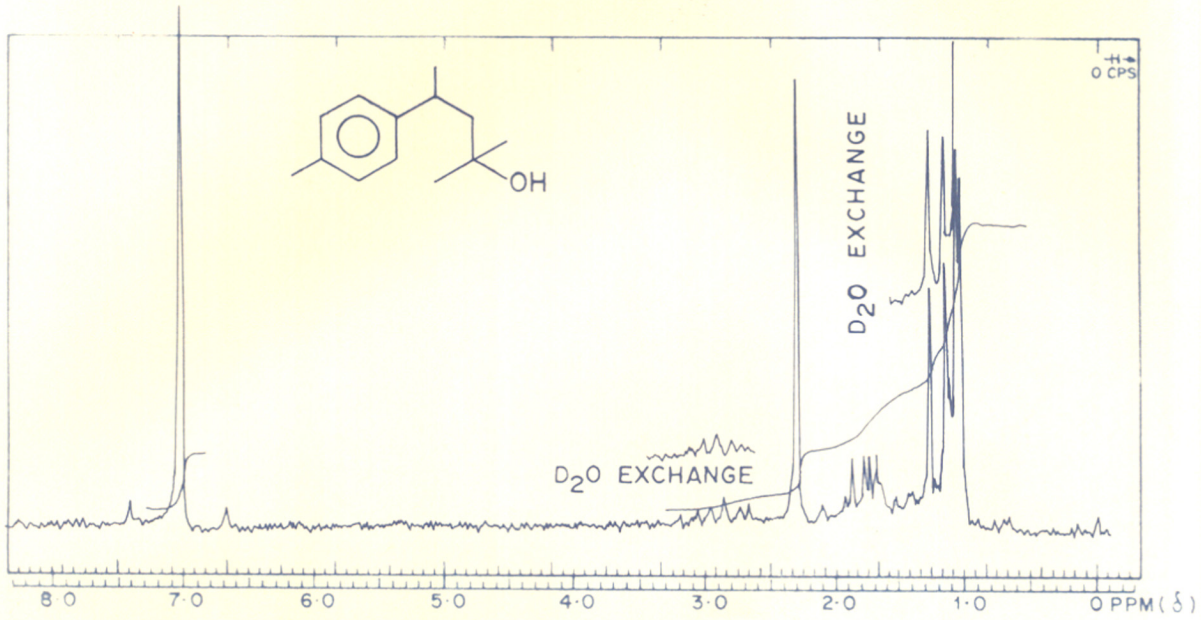
NMR SPECTRUM OF 3β,6-DIMETHYLINDANE-1β-OL (X)

(IN CCl_4)



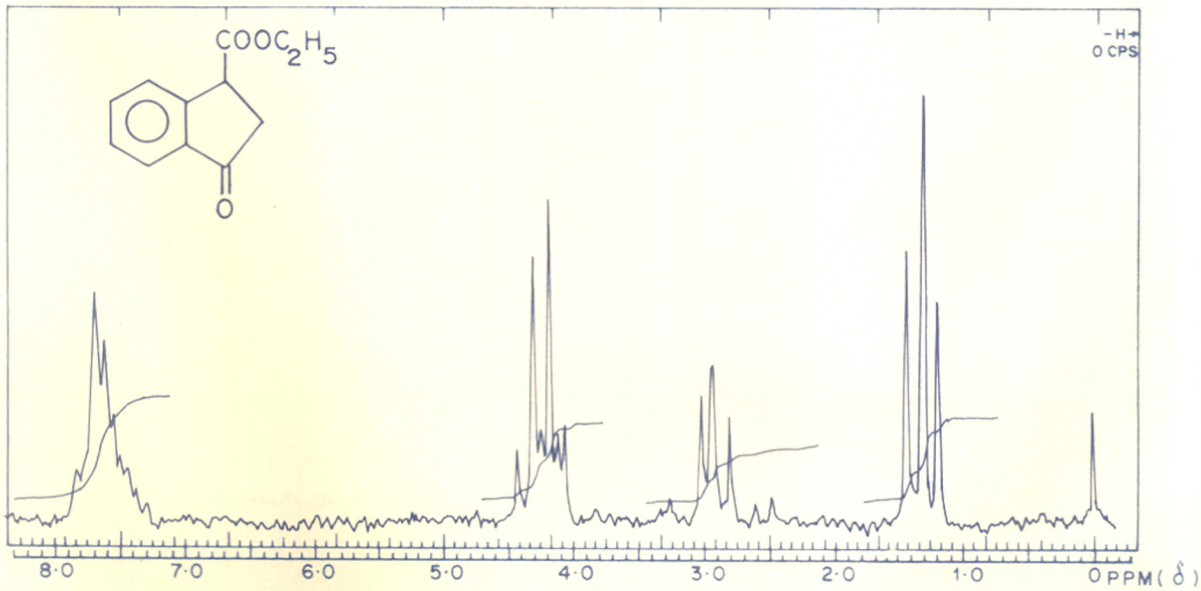
NMR SPECTRUM OF 3β,6-DIMETHYL-1β-ACETOXYINDANE (XIV)

(IN CCl_4)



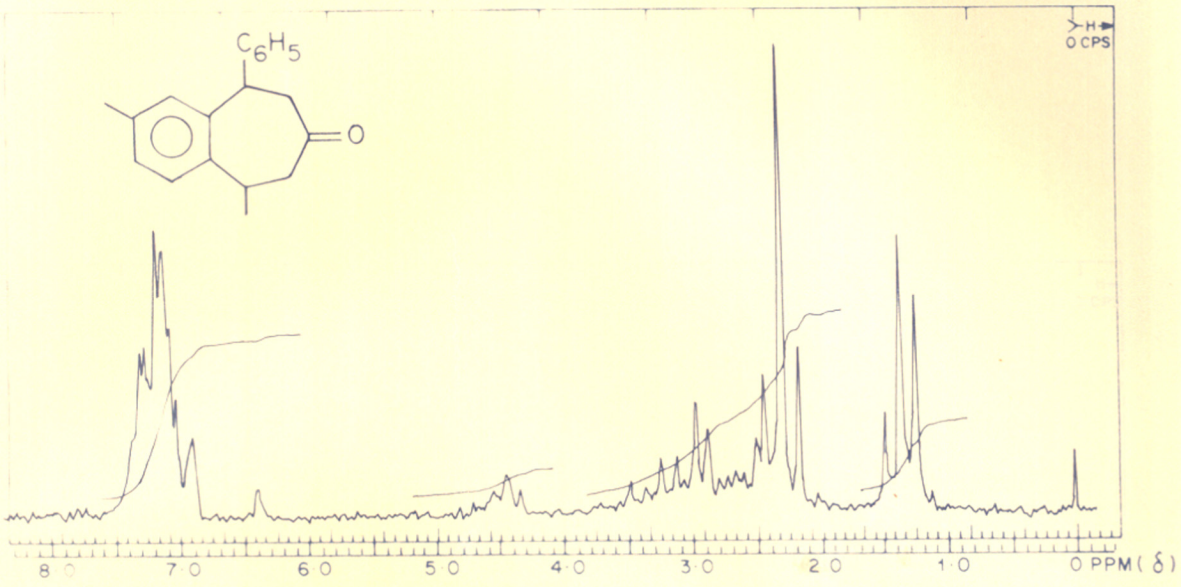
NMR SPECTRUM OF 2-METHYL-4-p-TOLYLPENTANE-2-OL (XVI)

(IN CCl_4)



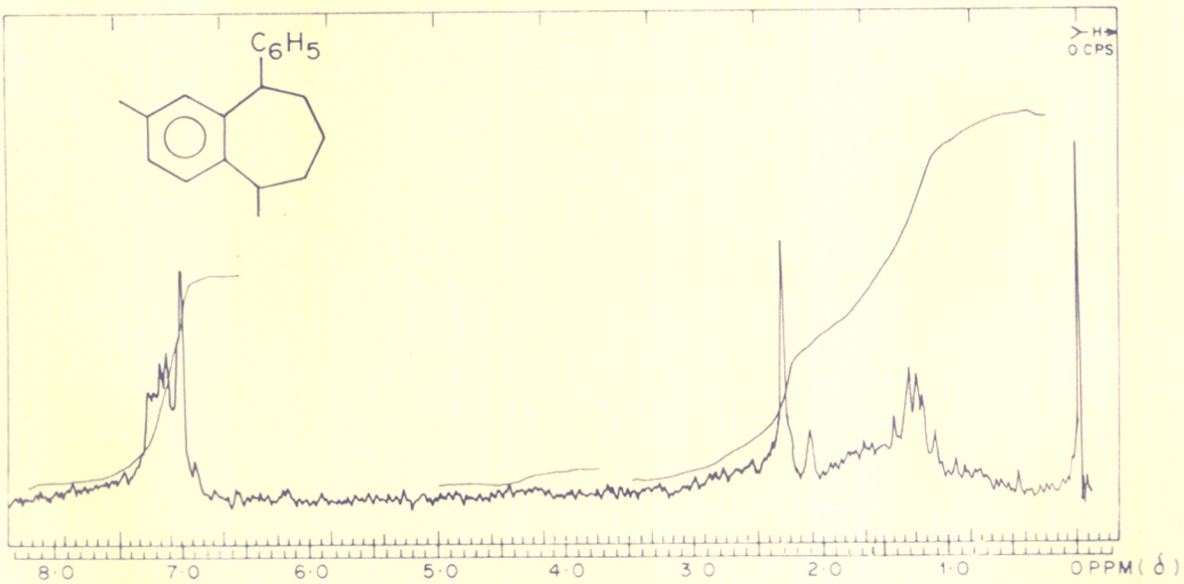
NMR SPECTRUM OF ETHYL ESTER OF 1-OXO-INDANE-3-CARBOXYLIC ACID(XXXVIII)

(IN CCl_4)



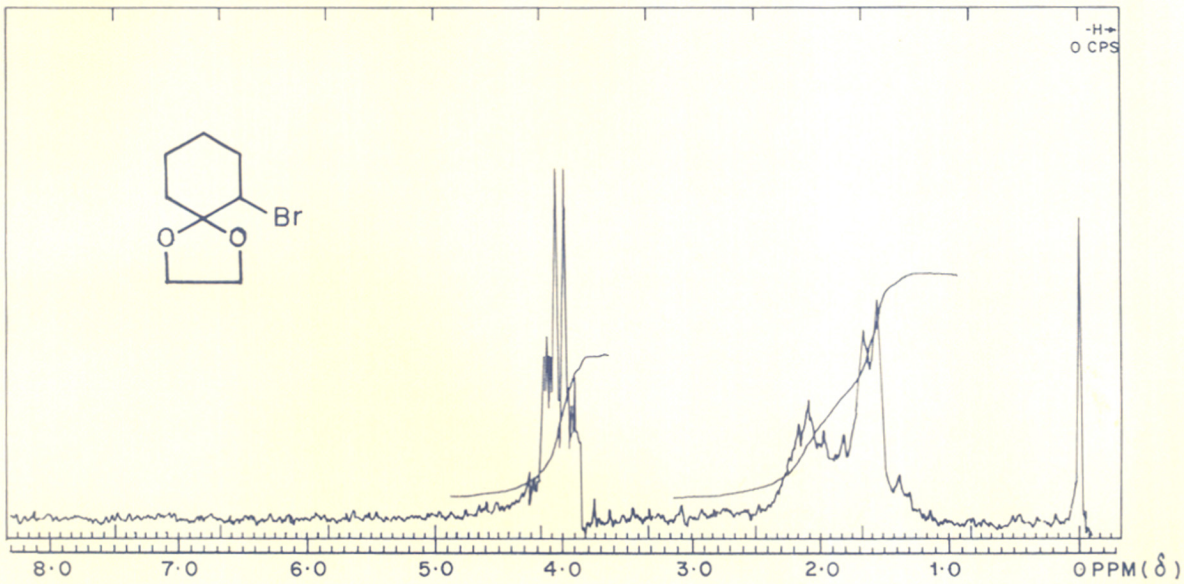
NMR SPECTRUM OF 2,5-DIMETHYL-9-PHENYL-7-OXO-BENZOSUBERANE (XXXII)

(IN CCl_4)

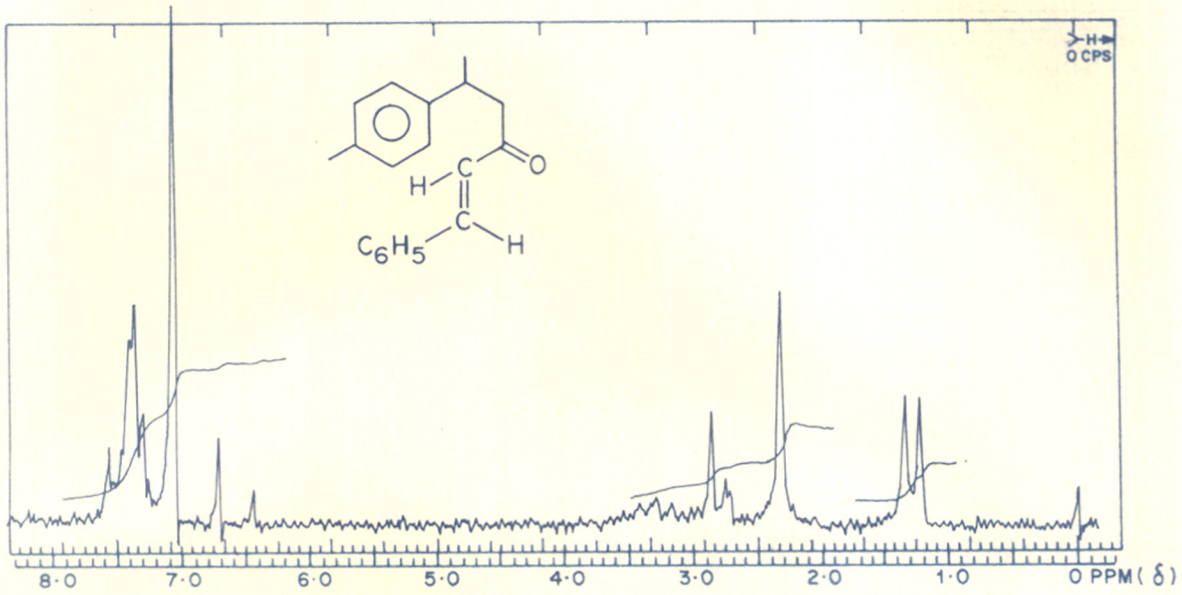


NMR SPECTRUM OF 2,5-DIMETHYL-9-PHENYLBENZOSUBERANE (XXXIV)

(IN CCl_4)

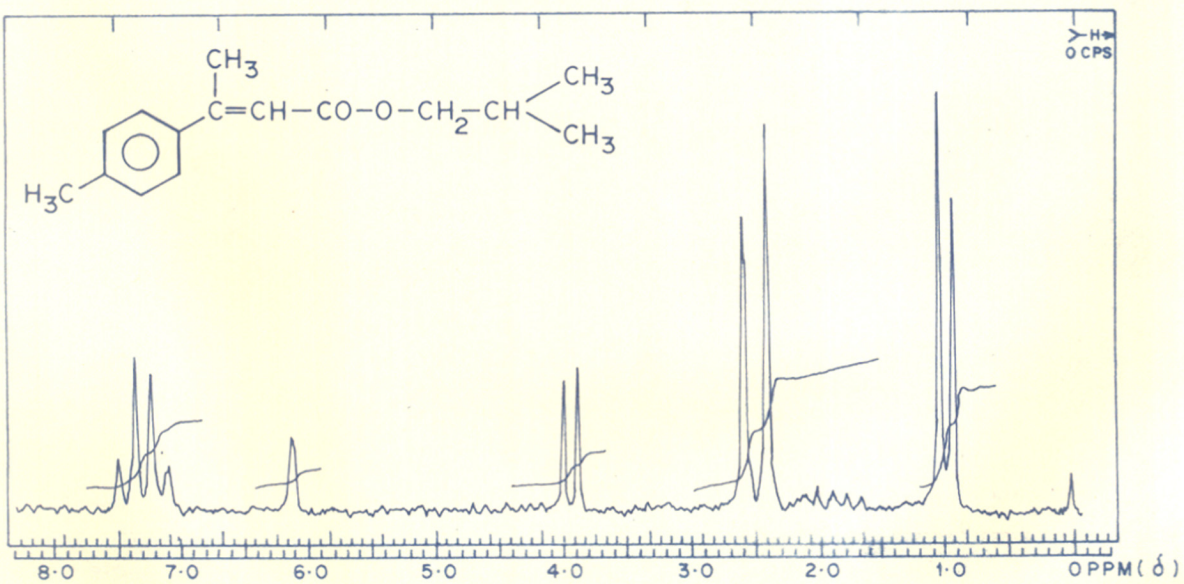


NMR SPECTRUM OF 1-ETHYLENEDIOXY-2 BROMOCYCLOHEXANE (XLIII)
(IN CCl_4)



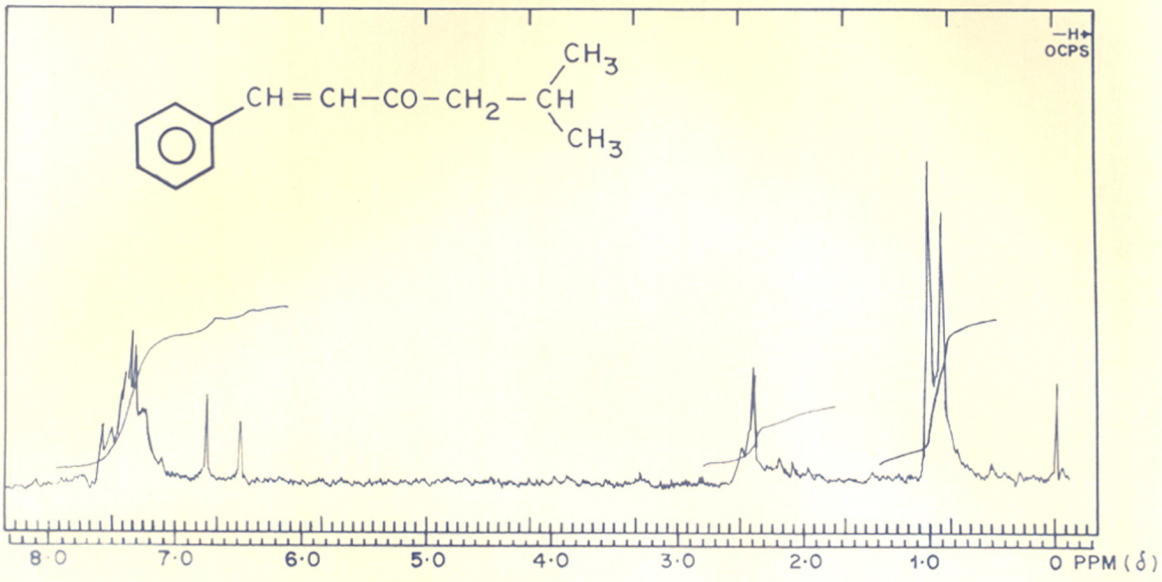
NMR SPECTRUM OF 1-PHENYL-5-p-TOLYLHEX-1-ENE-3-ONE (XXXI)

(IN CCl_4)

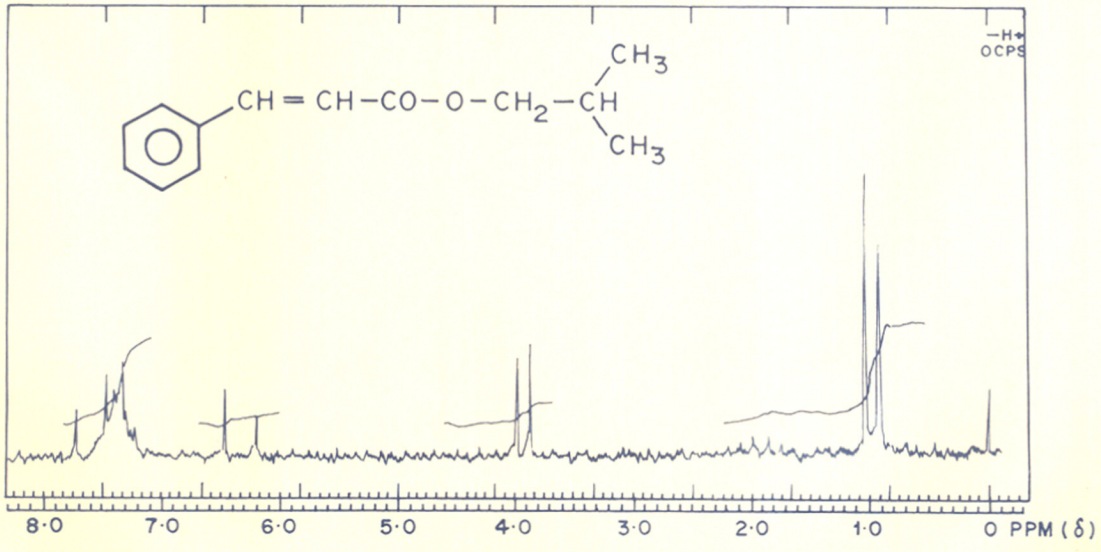


NMR SPECTRUM OF ISOBUTYL ESTER OF 3-p-TOLYLBUT-2-ENOIC ACID (LIX)

(IN CCl_4)

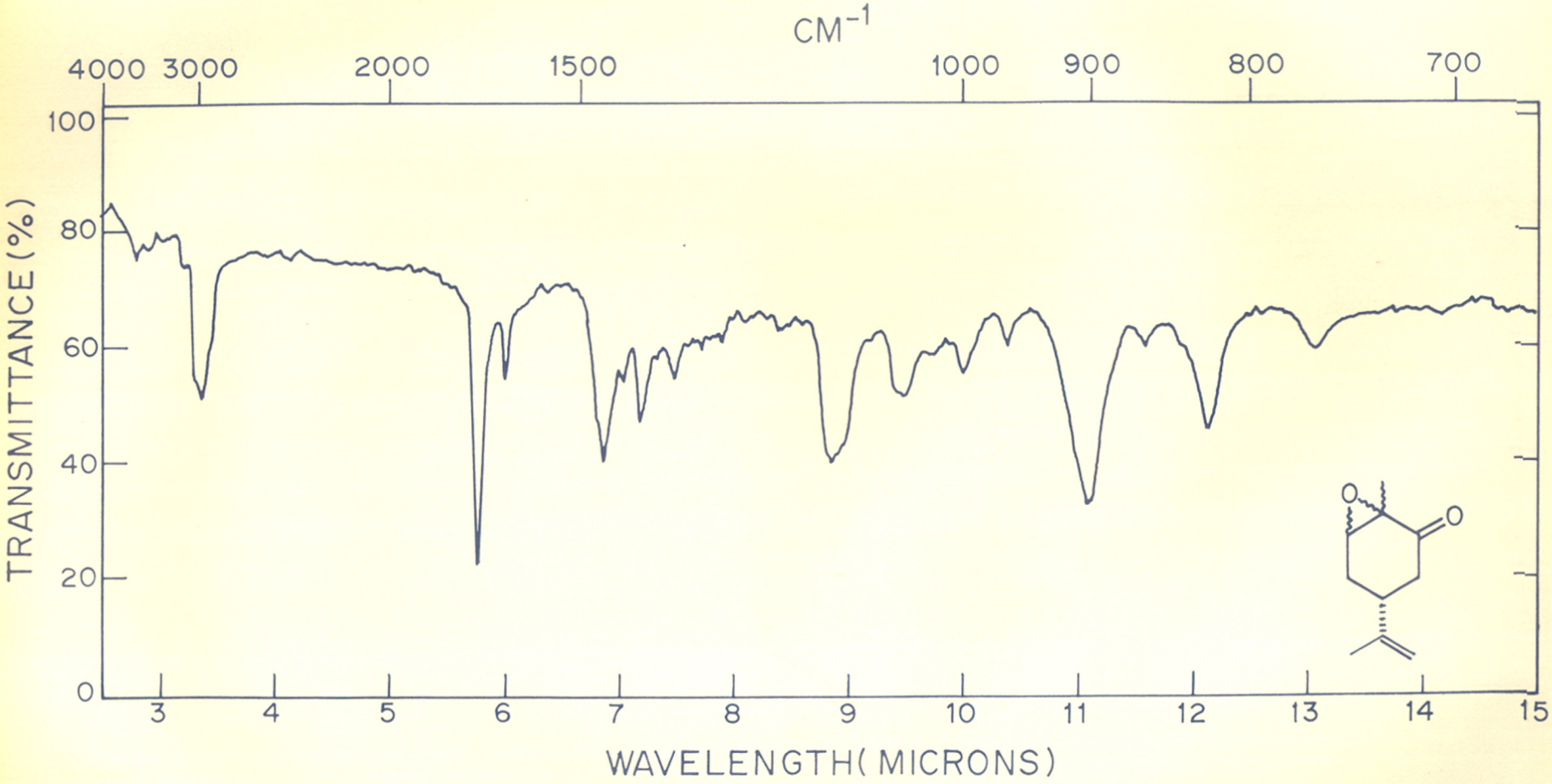


NMR SPECTRUM OF 2–METHYL–6–PHENYLHEX–5–EN–4–ONE (LXV)
(IN CCl_4)



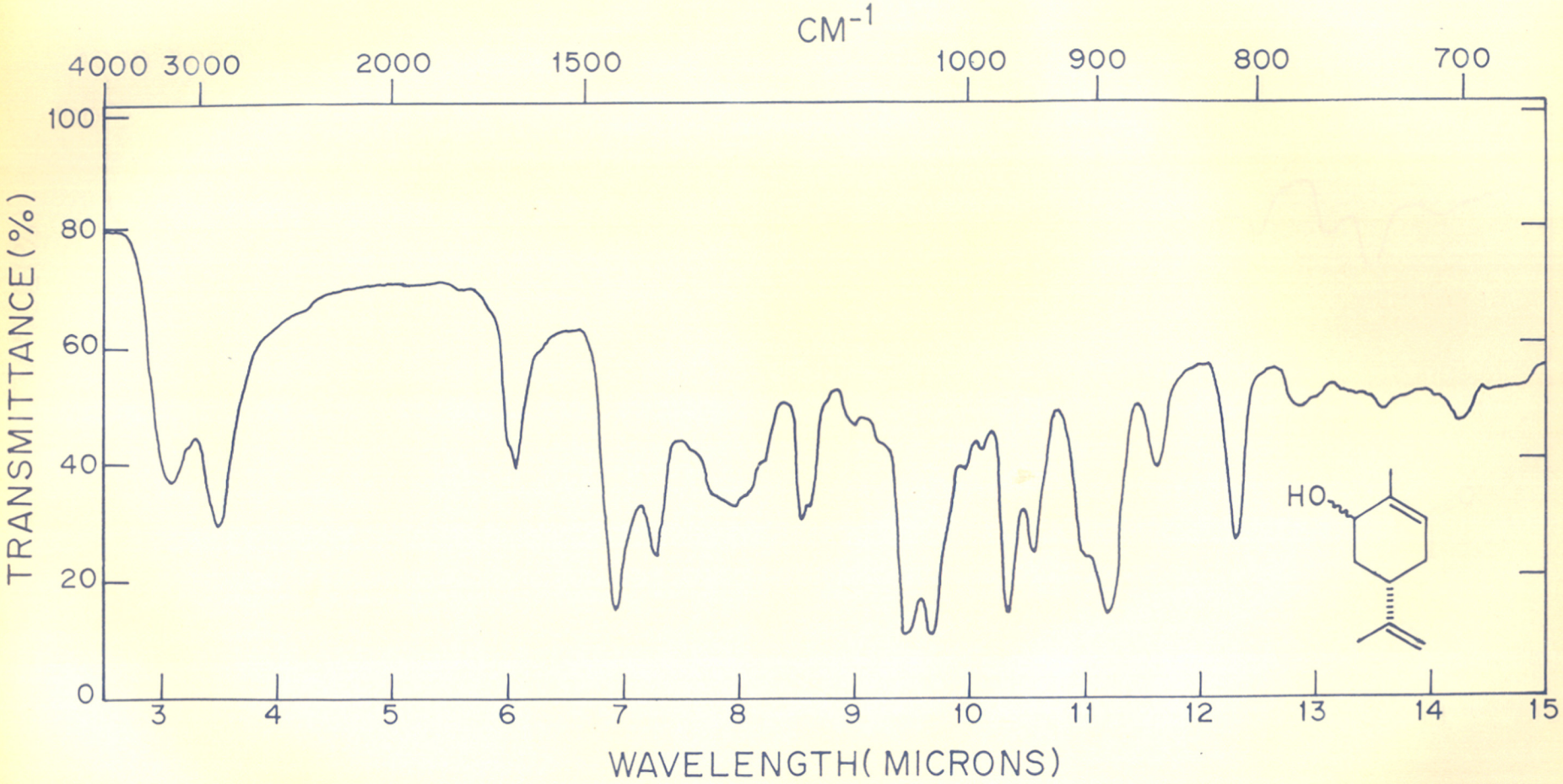
NMR SPECTRUM OF ISOBUTYL ESTER OF 3–PHENYLPROP–2–ENOIC ACID (LXII)
(IN CCl_4)

CHAPTER III



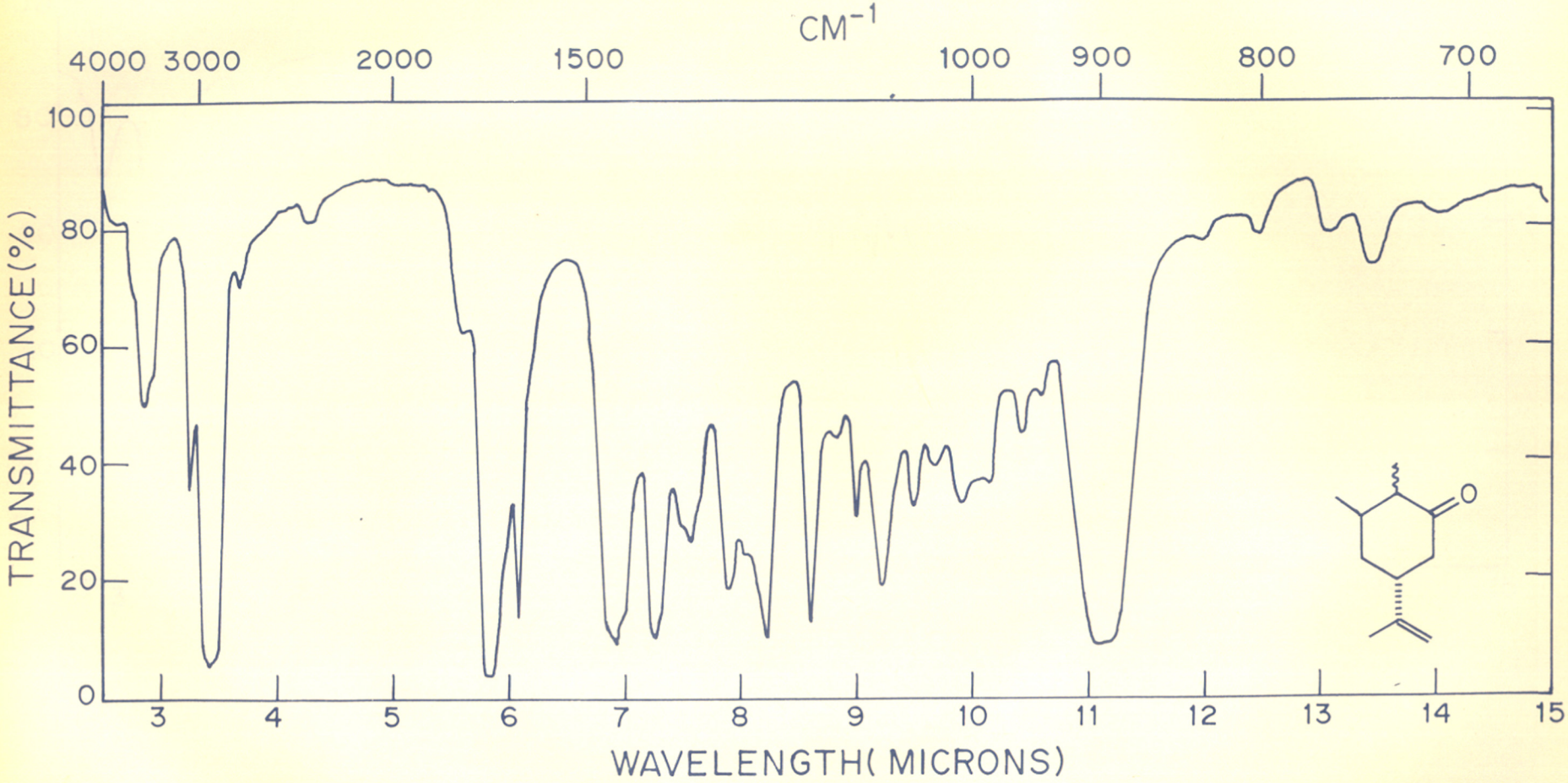
IR SPECTRUM OF 5 α -ISOPROPENYL-2 ξ -METHYL-2,3 ξ -OXIDOCYCLOHEXAN-1-ONE (II).

(LIQ. FILM)



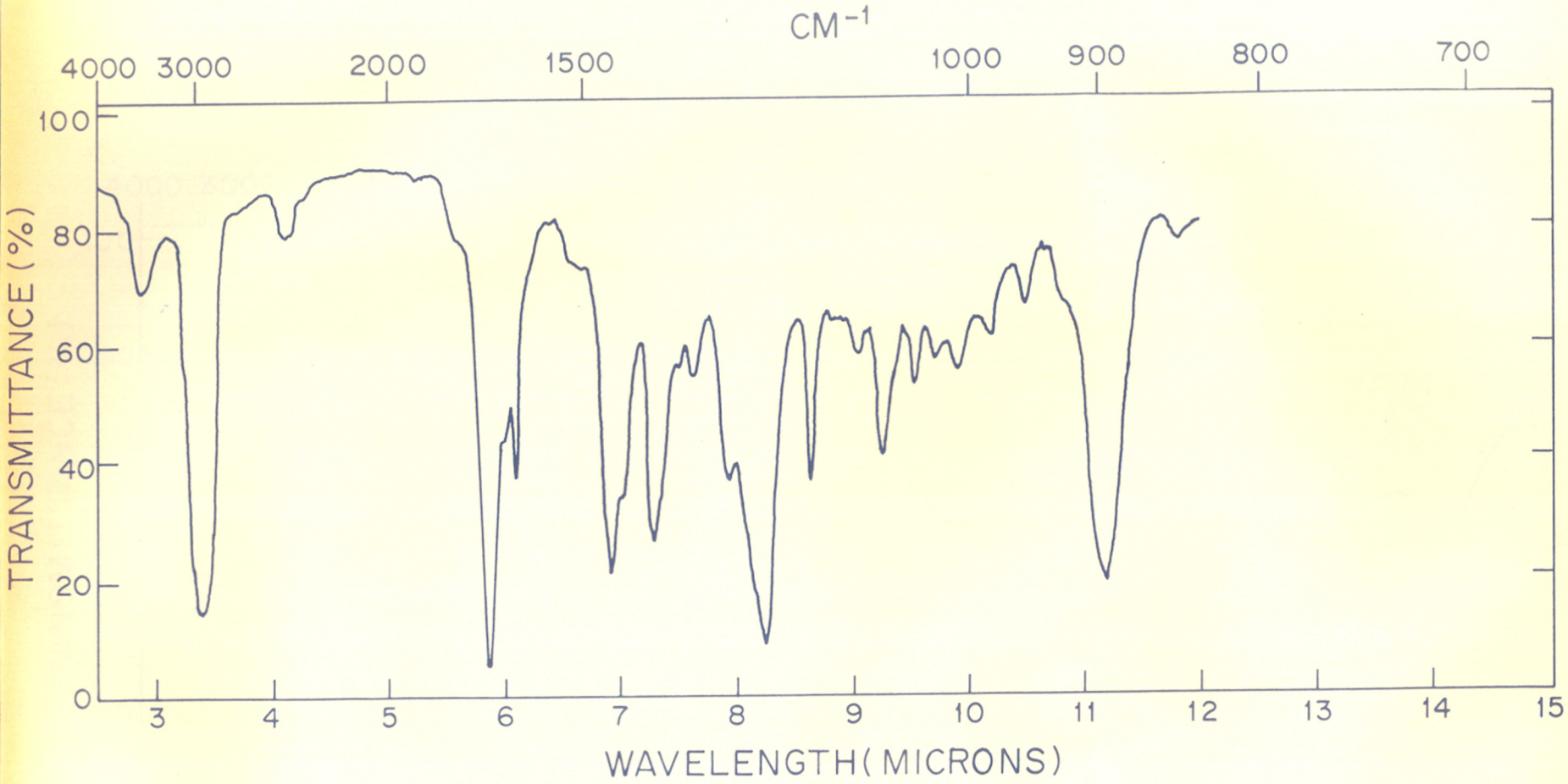
IR SPECTRUM OF 5α-ISOPROPENYL-2-METHYL-2-CYCLOHEXEN-1β-OL (V)

(LIQ. FILM)

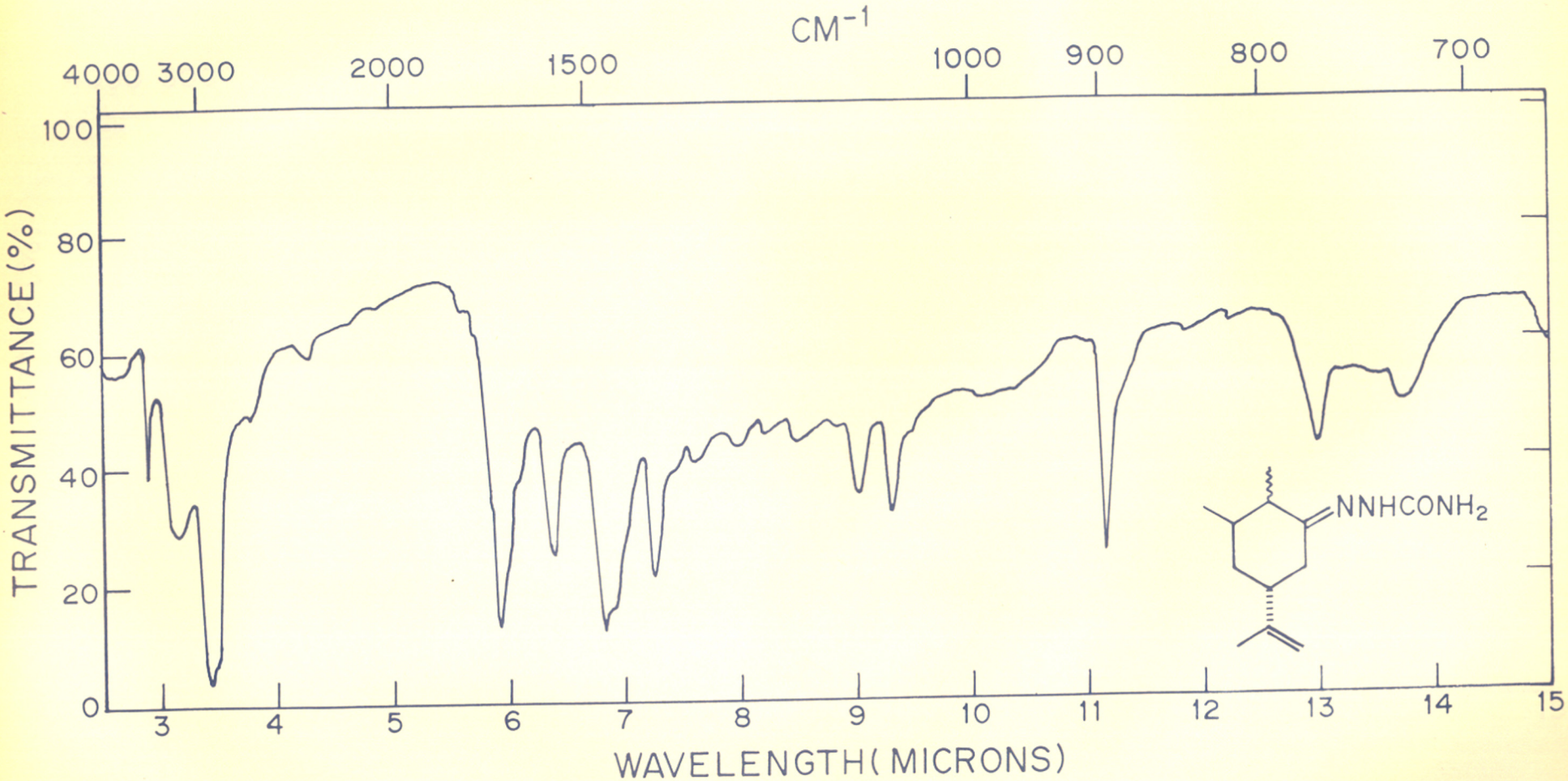


IR SPECTRUM OF 5α-ISOPROPENYL-2ξ,3β-DIMETHYLCYCLOHEXAN-1-ONE (X)

(LIQ. FILM)

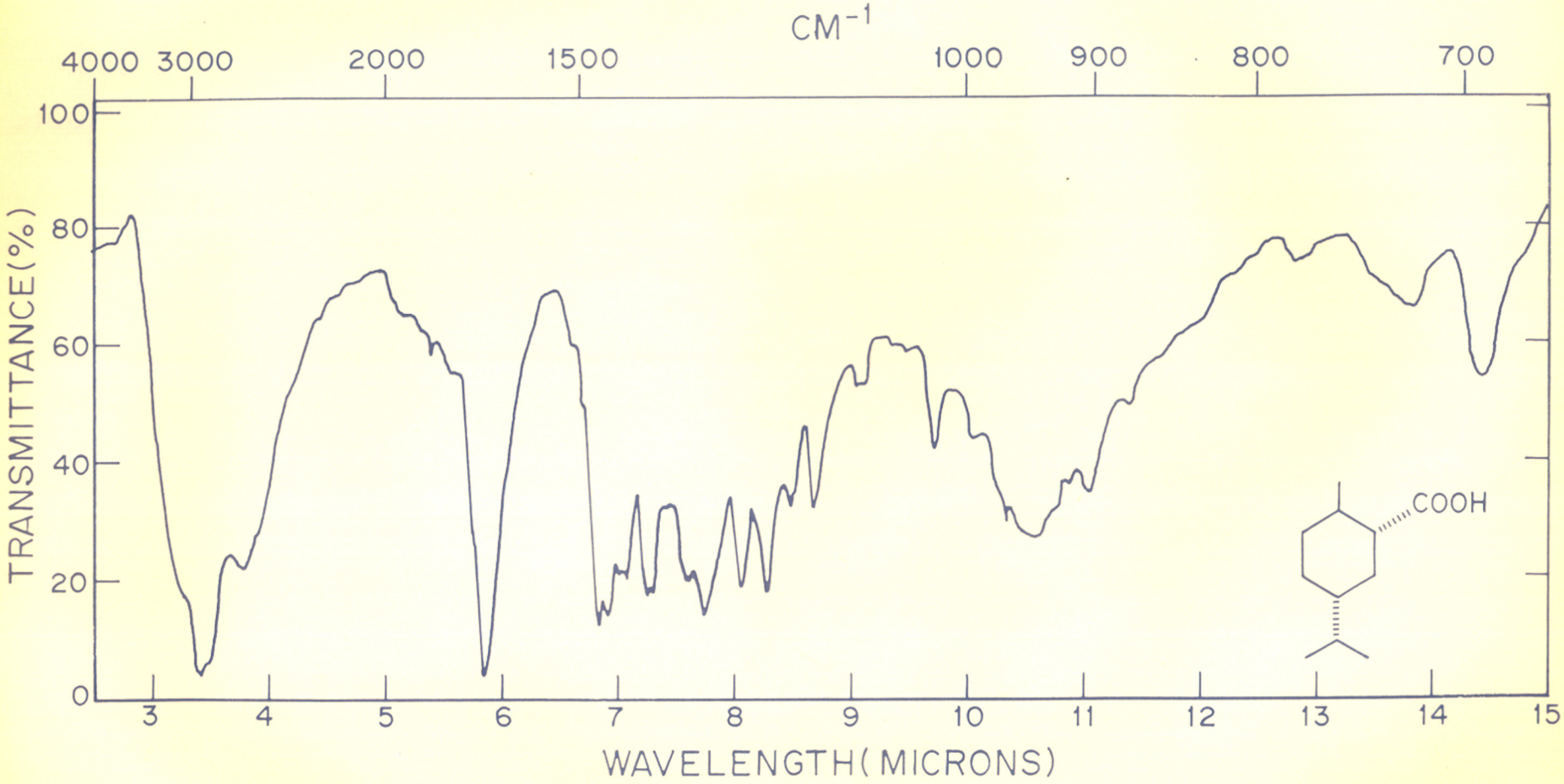


IR SPECTRUM (LIQ·FILM) OF METHYLCARVONE (Ret. time 3'-4"), P. 122



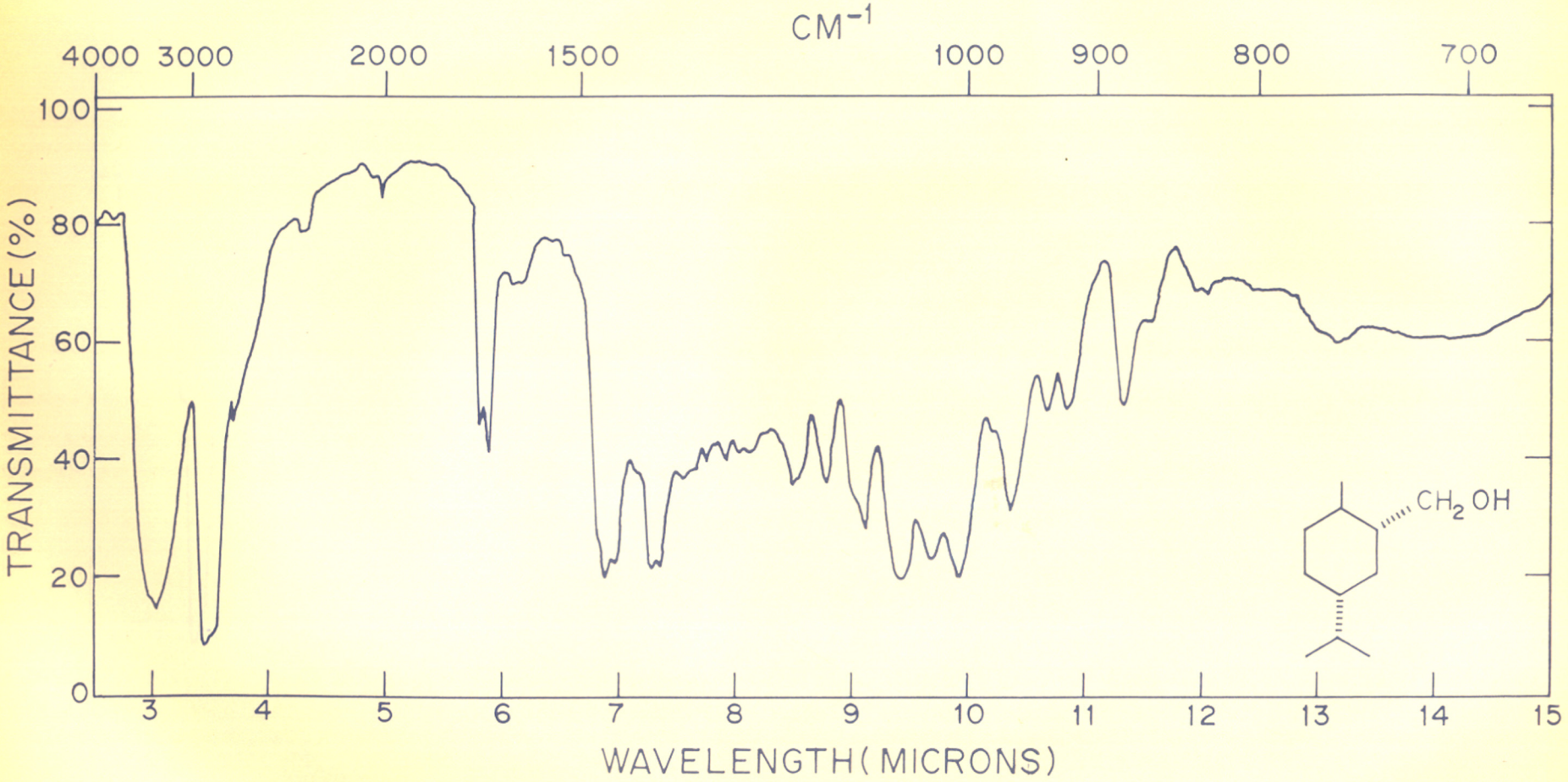
IR SPECTRUM OF 5α-ISOPROPENYL-2ξ,3β-DIMETHYLCYCLOHEXAN-1-ONE SEMICARBAZONE (XIII)

(IN NUJOL)



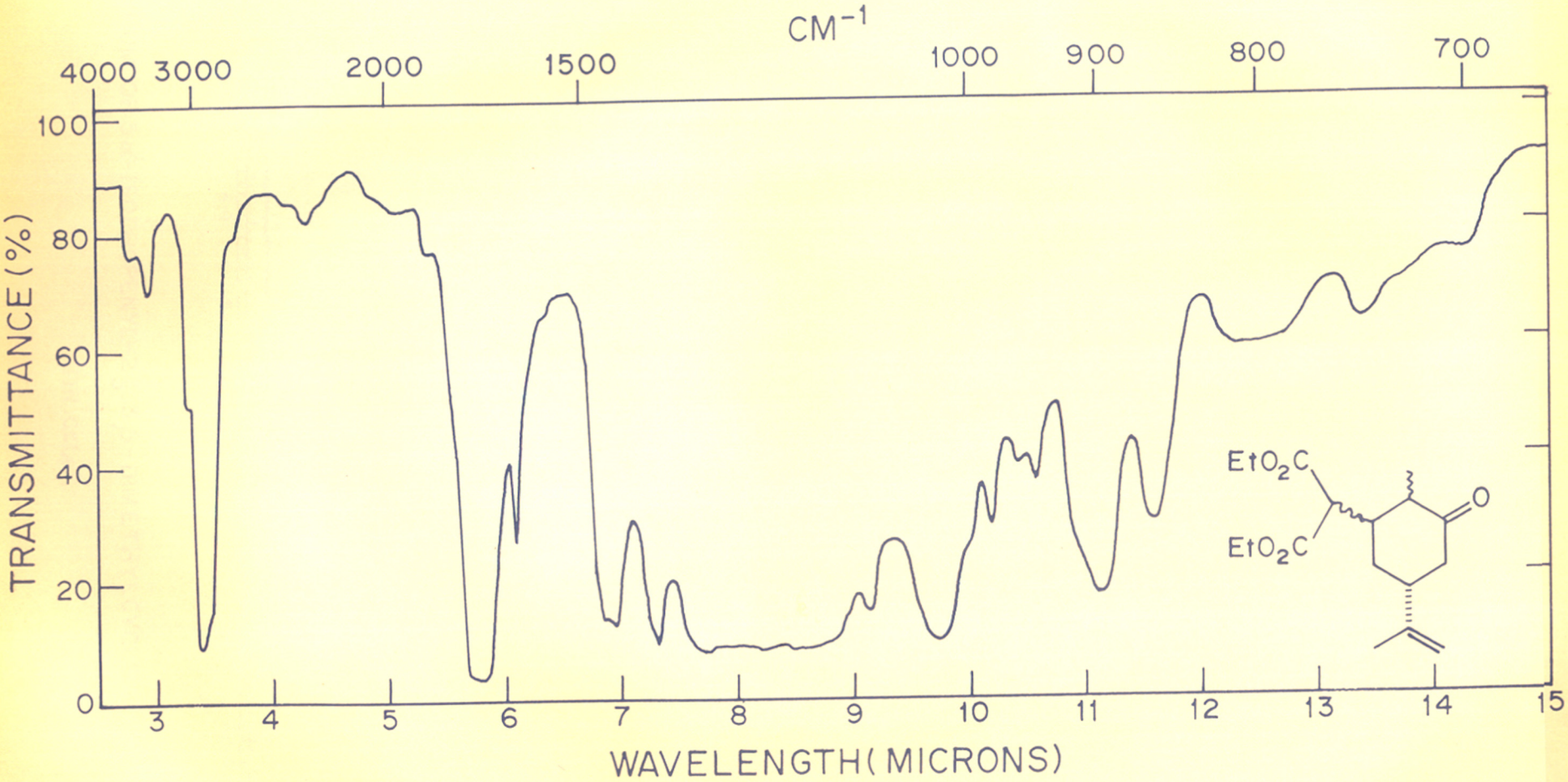
IR SPECTRUM OF 5α-ISOPROPYL-2β-METHYLCYCLOHEXANE-1α-CARBOXYLIC ACID (XXIII)

(IN NUJOL)



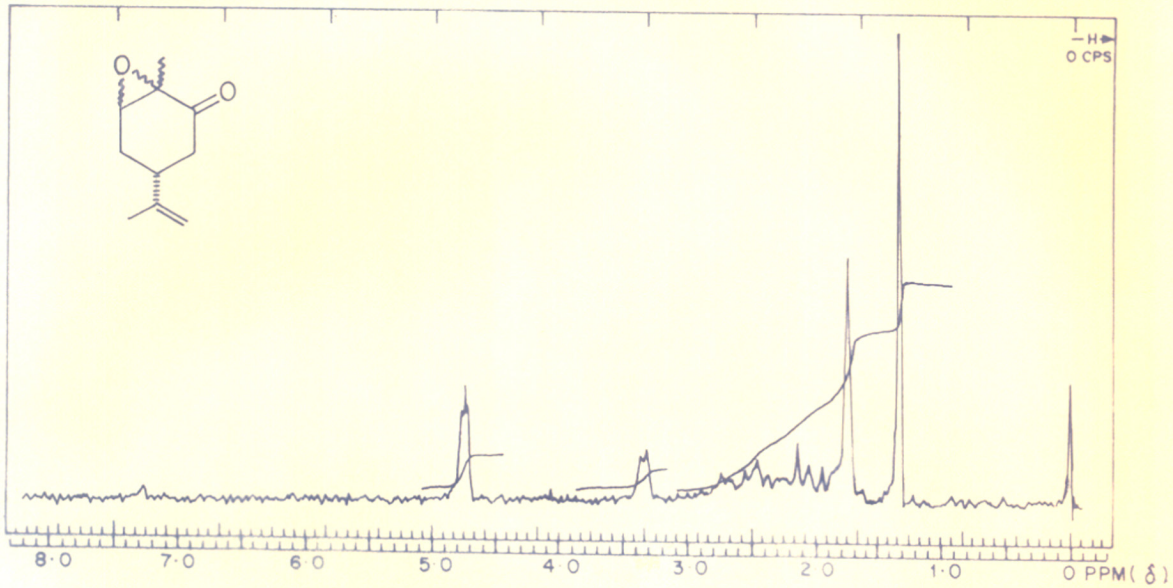
IR SPECTRUM OF 5α-ISOPROPYL-2β-METHYLCYCLOHEXANE-1α-METHANOL (XXV)

(LIQ·FILM)



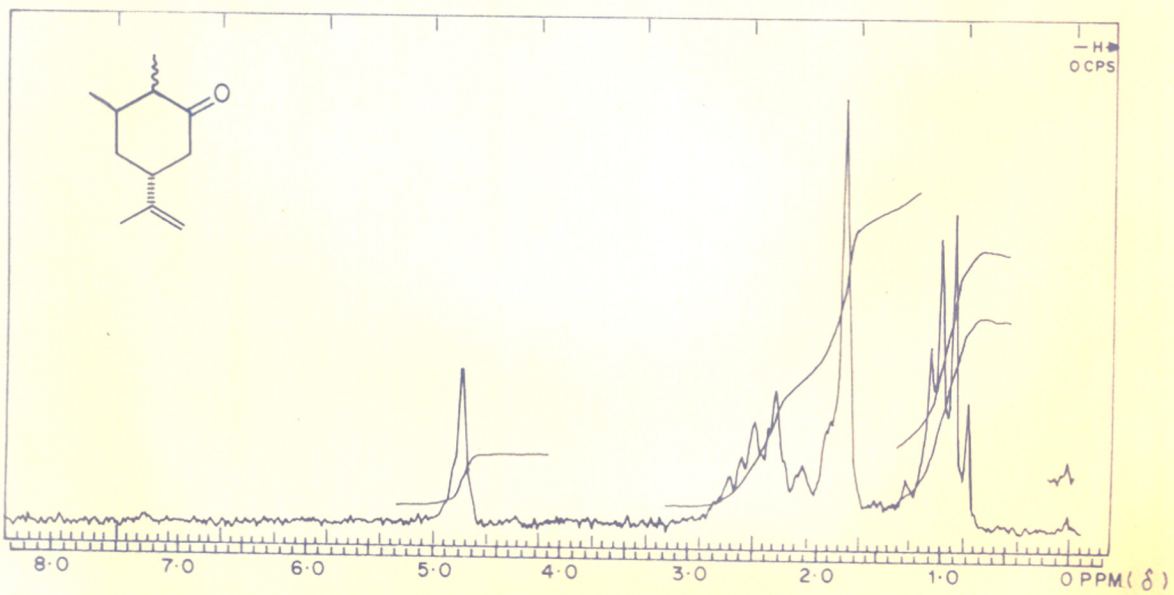
IR SPECTRUM OF DIETHYL ESTER OF 5α-ISOPROPENYL-2ξ-METHYL-3-OXOCYCLOHEXYLMALONIC ACID (XXXIV)

(LIQ. FILM)



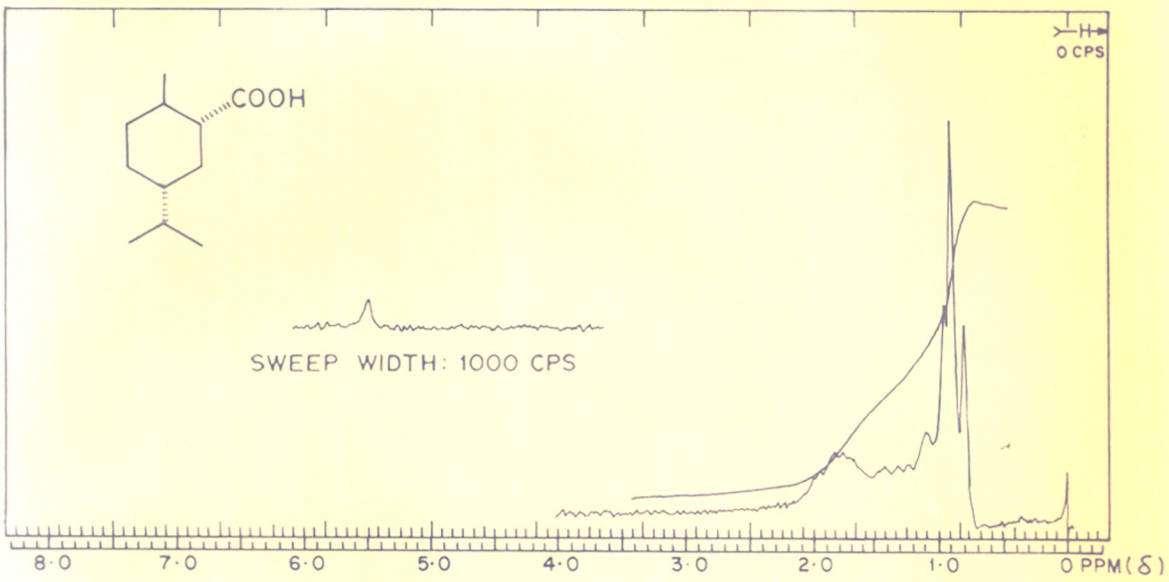
NMR SPECTRUM OF 5 α-ISOPROPENYL-2 ξ-METHYL-2,3 ξ-OXIDOCYCLOHEXAN-1-ONE (II)

(IN CCl_4)



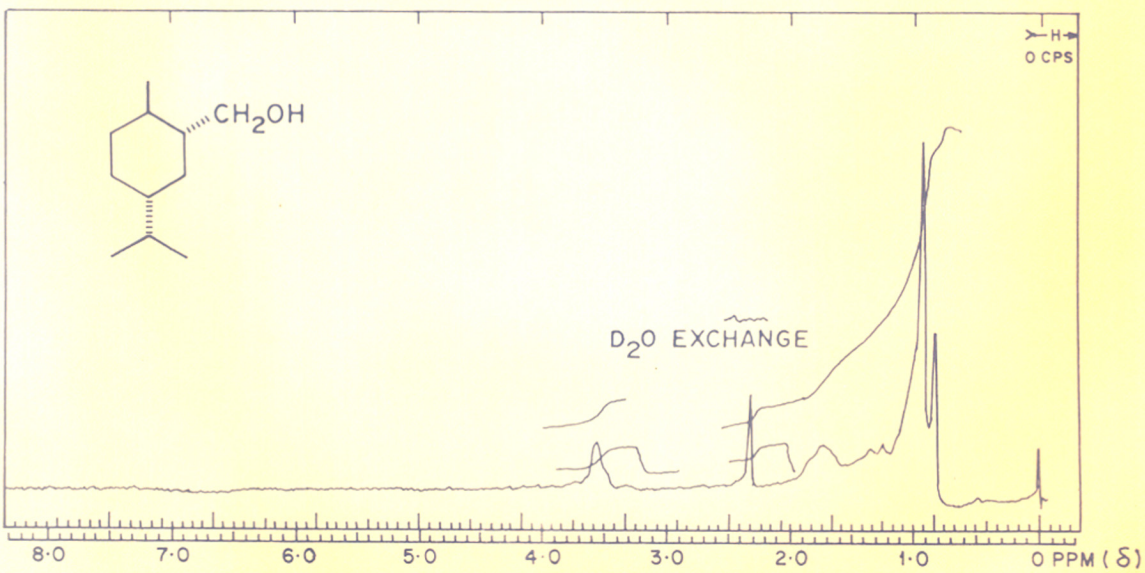
NMR SPECTRUM OF 5α-ISOPROPENYL-2 ξ,3 β-DIMETHYLCYCLOHEXAN-1-ONE (X)

(IN CCl_4)



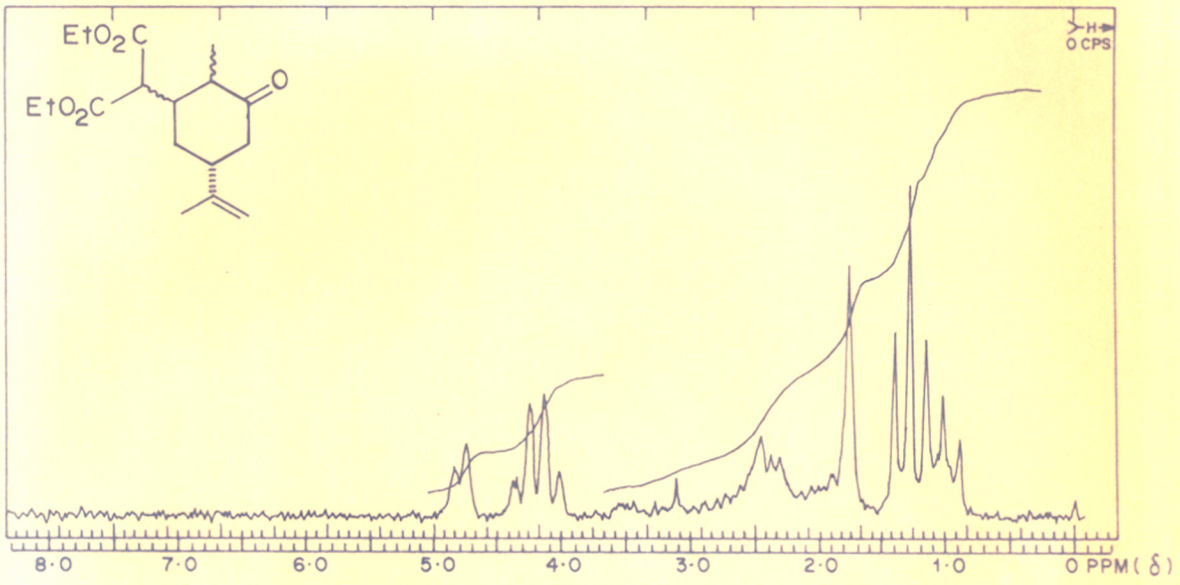
NMR SPECTRUM OF 5 α-ISOPROPYL-2β-METHYLCYCLOHEXANE-1α-CARBOXYLIC ACID (XXIII)

(IN CCl_4)



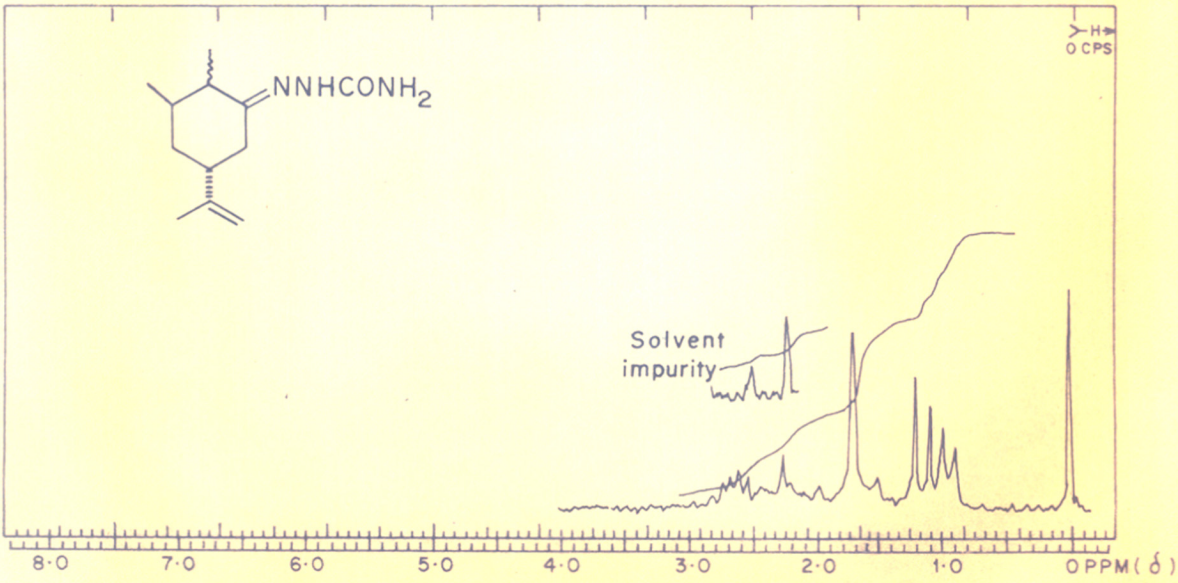
NMR SPECTRUM OF 5 α-ISOPROPYL-2β-METHYLCYCLOHEXANE-1α-METHANOL (XXV)

(IN CCl_4)



NMR SPECTRUM OF DIETHYL ESTER OF 5α-ISOPROPENYL-2ξ-METHYL-3-OXOCYCLOHEXYLMALONIC ACID (XXXIV)

(IN CCl_4)



NMR SPECTRUM OF 5α-ISOPROPENYL-2ξ,3β-DIMETHYLCYCLOHEXAN-1-ONE SEMICARBAZONE (XIII)

(IN PYRIDINE)

A C K N O W L E D G M E N T S

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EMINA SISKOVIC

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