CHAPTER-IV

SYNTHESIS OF A JH MIMIC BASED ON (+)-LIMONENE

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ABSTRACT

This Chapter describes the synthesis of methyl 10,11-epoxy-8,13-cyclo-7-methylene-3,11-dimethyl-tridec-2(E)-enoate (16) from (±)-limonene. It has the same structural features as JH-II except that the 8:13-carbons are linked as in cyclohexane ring and C_6-double bond is shifted to C_7(15) position. The synthesised compound was found ten times as active as the reference compound, farnesyl methyl ether.

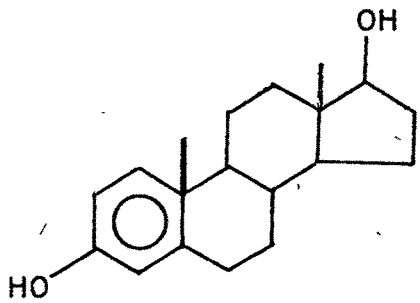
SYNTHESIS OF A JH MIMIC BASED ON (+)-LIMONENE

INTRODUCTION

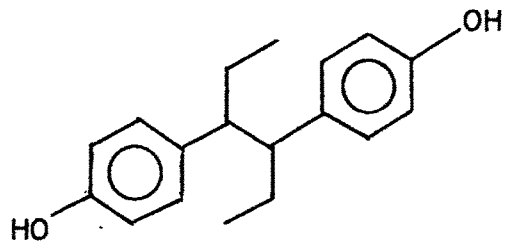
The biological study of natural products, their derivatives and synthetic analogs has firmly established the early hypotheses about possible relationship between chemical structure and over-all biological profile. The observation that certain structural units of the biologically active compounds are also to be found in those of other compounds having similar properties provided a guiding thought in mapping the structure of further compounds with analogous activities, hopefully more potent, more specific, or less toxic. Even an apparently very subtle variation in chemical structure may thus uncover newer biological effects.

One of the interesting modifications could be the opening of cyclic or closing of acyclic structures[1] thereby arriving at compounds that have comparable shapes/ conformations. Potent estrogens are among the best known examples of this concept. The natural estrogenic hormone (1) can be simulated by the synthetic diethyl-stilbestrol (2). The latter is about as active as the natural hormone and is much more potent than its tetra-cyclic analog with two terminal phenolic rings. The

central double bond of (2) seems to hold the two ethyl

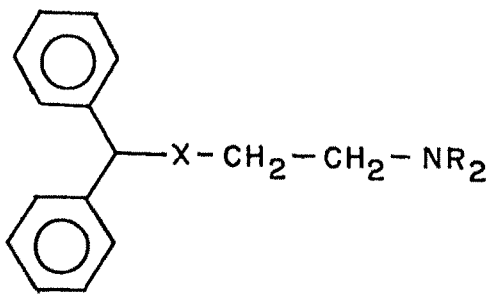


(1)



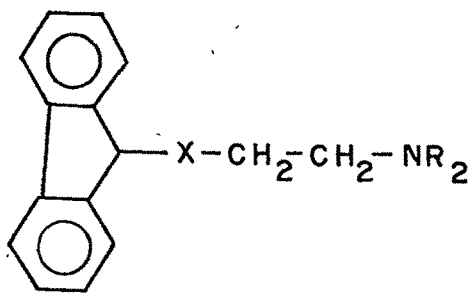
(2)

groups in an optimal position[1e]. Tying back the aromatic rings of diphenyldramine (3), an antihistaminic, give a fluorene analog (4) with reduced antihistaminic activity[1d,1e]. However, the same transformation steps up (weak) activity in the series of anticholinergic diethylaminoethyl esters (5 and 6).



3 : X = O

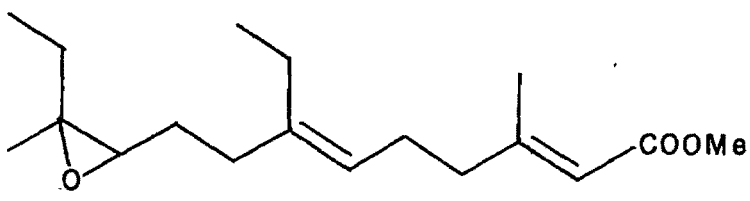
5 : X = CO_2



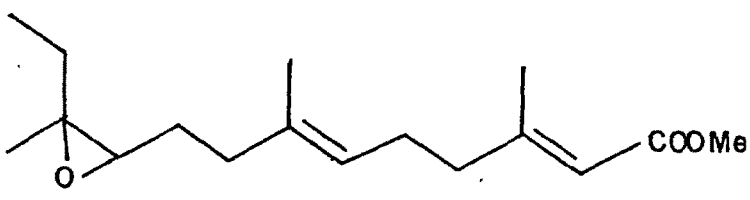
4 : X = O

6 : X = CO_2

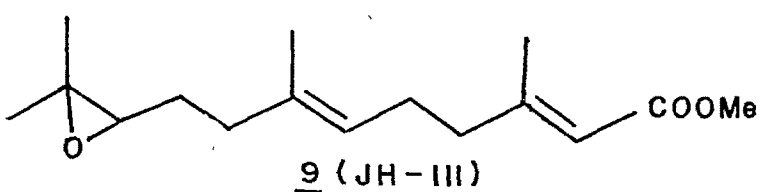
Although, the chemical structures of the three known natural juvenile hormones (JH-I, JH-II and JH-III; 7-9) of Cecropia do provide considerable helpful information to the chemist for the synthesis of active analogs, these acyclic structures reveal little about the shape requirements of the receptor.



7 (JH-I)



8 (JH-II)



9 (JH-III)

When a compound elicits a particular biological effect, it is accepted that the compound adopts a particular conformation during the process of binding to a specific receptor protein. Thus, a particular shape of say, the

Juvenile hormone, though impossible to predict, is nontheless important to an understanding of hormonal action. However, some insight can be gained by using the previous concept of closing part of acyclic system and thereby restricting the number of possible conformations. Such an approach to Cecropia juvenile hormones has resulted in the syntheses of a few JH-analogues in which cyclopropane[2], cyclobutane[3] (10), cyclopentane[4,5] (11, 12) and cyclohexane[4,6,7] (14,15) rings have been incorporated (Chart I). However, the data generated so far have not been sufficient for the emergence of any clear postulate regarding the conformation that the acyclic juvenile hormone molecule adopts at the time of binding to the receptor site.

RESULTS AND DISCUSSION

The present study was aimed at synthesising C_6-C_{13}-cyclo JH-II (16) and evaluating its JH-activity. The fact that the double bond at C-6 is not an essential feature[8-12] for an analogue to show JH activity and reasons of expediency led us to restrict our efforts in synthesising this $\Delta^{7(15)}$ isomer instead of the Δ^{6}

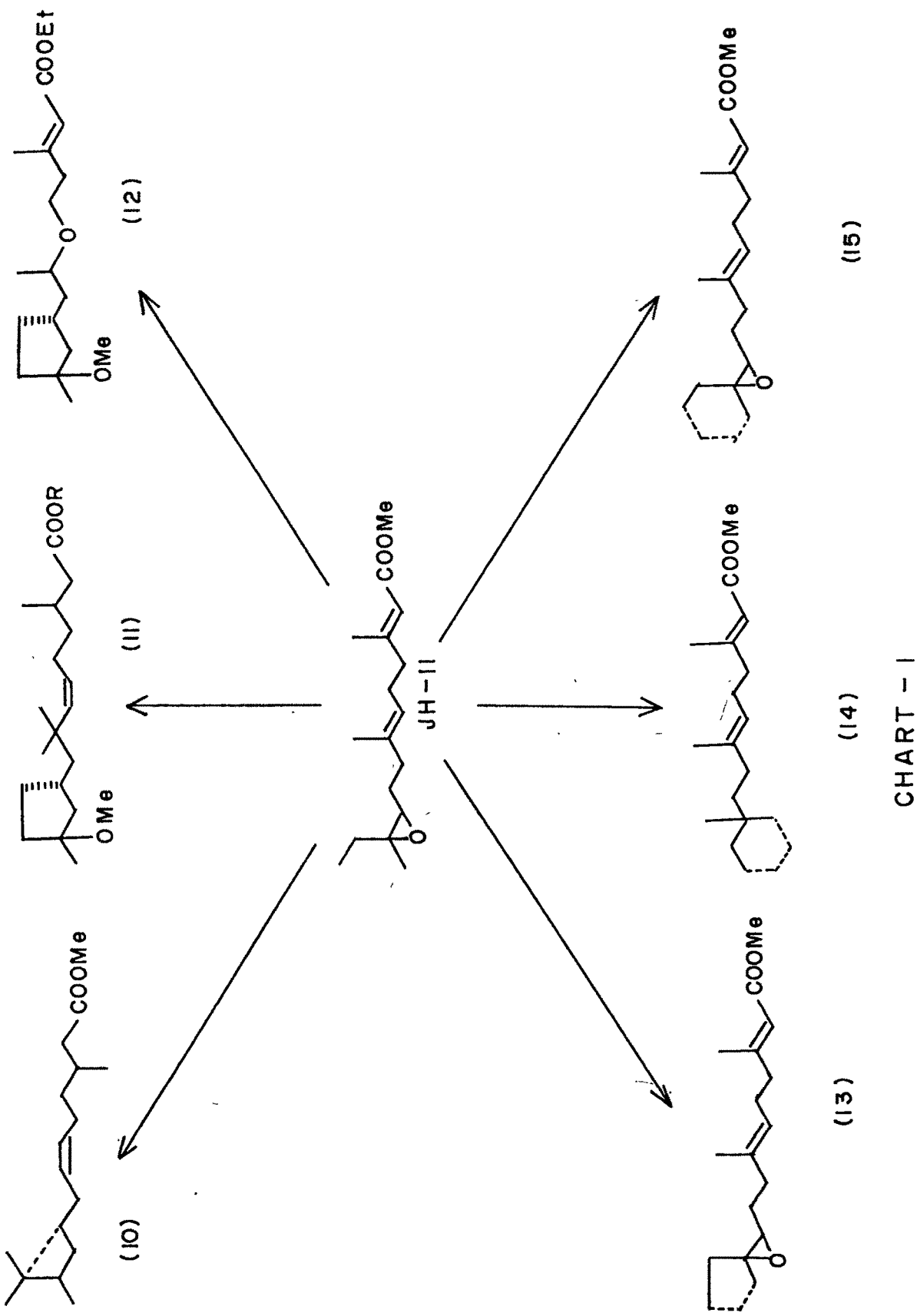
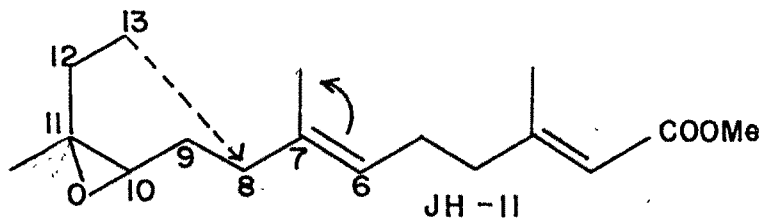
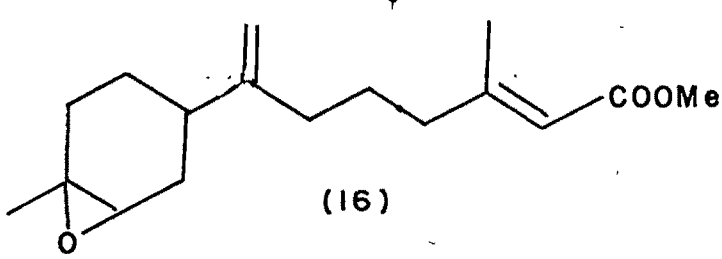

COOEt
O
OMe
(12)
COOR
OMe
(11)
COOMe
JH-11
O
COOMe
(10)
COOMe
(15)
COOMe
(14)
COOMe
O
(13)

CHART - I

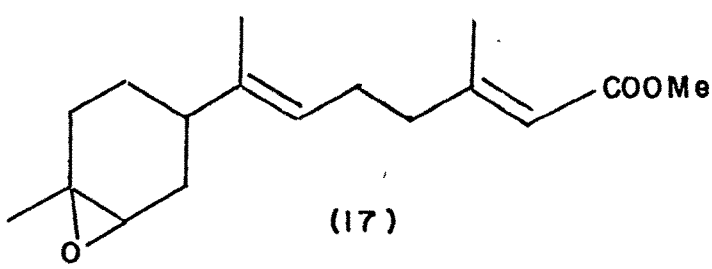
compound (17) itself. Other studies[13] have revealed that there is no significant difference in JH activity between isomeric analogues having the double bond at C-6 and those having it at C-7(15) positions. Structure (16) represents a molecule having the same number of carbon atoms and functionalities as JH-II but having the conformational mobilities of part of the acyclic system (C_8 to C_{13}) restricted to those available for a cyclohexane ring and having the double bond at C-6 shifted to C-7(15) position.



JH-II



(16)



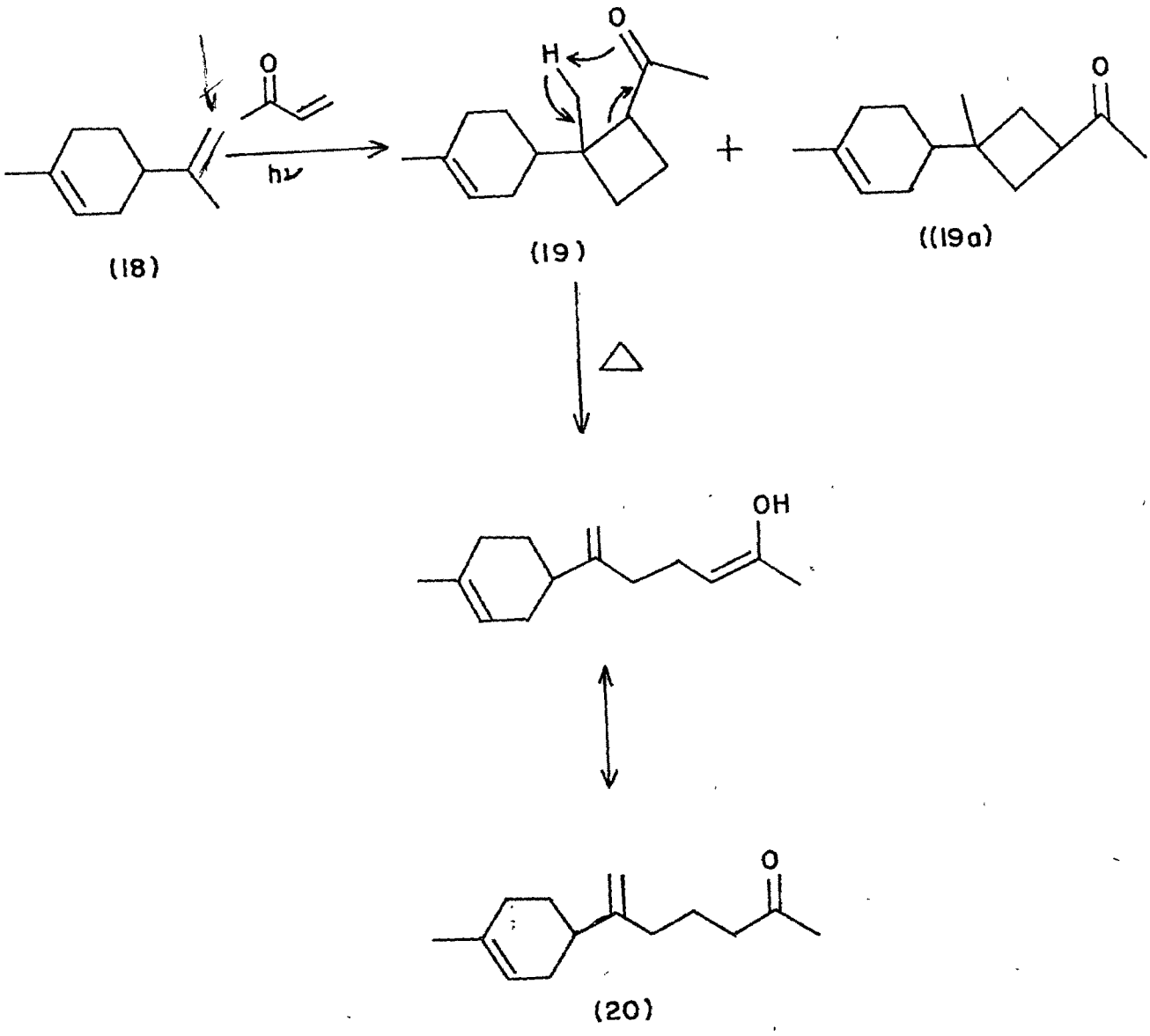
(17)

The strategy adopted for the synthesis of (16) consisted of exploiting all the structural features of (+)-limonene and build up the remaining six-carbon chain in units of four and two. A four-carbon extension with a suitable functionality at the other end (to help further extend the chain by two-carbon unit) can possibly be achieved in several ways of which the following two were considered:

i) Photochemical [2 + 2] cycloaddition of methylvinyl ketone to the C-8 double bond of (+)-limonene (18) followed by the thermolytic opening of the cyclobutane compound formed (19) (Chart II).

ii) Lewis acid catalysed or thermal ene reaction of (+)-limonene with methyl vinyl ketone (Chart III).

Once the key intermediate, the C-14 ketone 20, is prepared, further two-carbon extension can be conveniently carried out by the modified Wittig reaction. Selective epoxidation of the isolated terminal double bond in 21 would then afford the desired ester (16) (Chart III).



(18) (19) ((19a) (20)

CHART – II

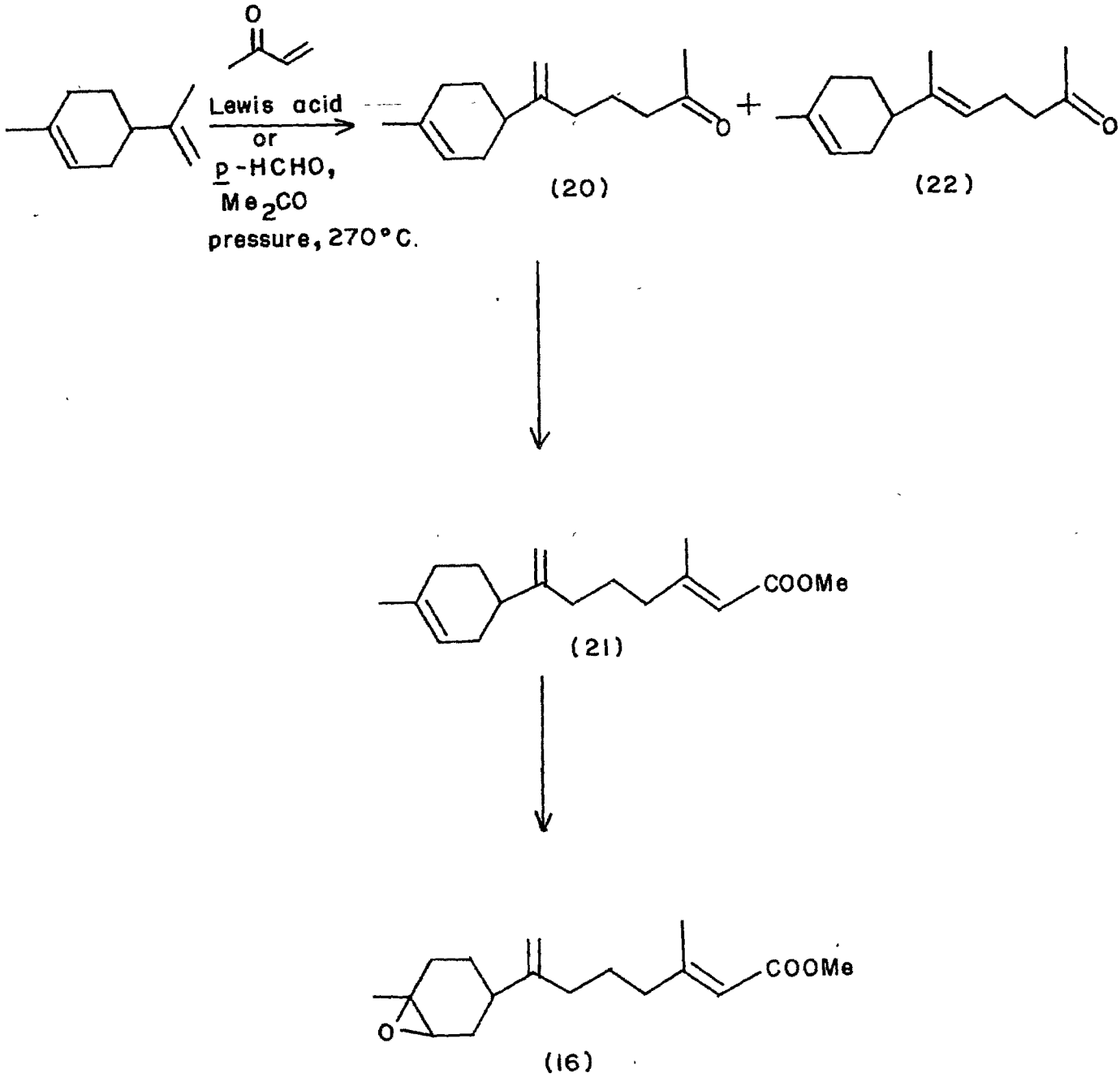

O
Lewis acid
or
p-HCHO,
Me2CO
pressure, 270°C.
(20)
(22)
COOMe
(21)
COOMe
O
(16)

CHART - III

Synthesis of the C_{14} ketone (20)

1) Photochemical [2 + 2] cycloaddition

Addition of an olefin to the double bond of an α,β-unsaturated ketone giving a cyclobutyl derivative is an important photochemical process of wide utility[14]. The reactive state in these cycloadditions of enones is believed to be the $n-\pi^*$ triplet. Generally, the α-carbon of the enones becomes attached to the most nucleophilic carbon of the double bond to form the cyclobutane ring[15,16].

Although a large volume of data on photochemical cycloadditions of different olefins with cyclic enones such as cyclopentenones, cyclohexanones, 2-acetyl cycloalkenones etc. is available, such reactions using acyclic enones as the substrate have not been well worked out so far[14-16]. Cycloaddition of methyl vinyl ketone to (+)-limonene (18) could be expected to give the head-to-head adduct 19 preferentially which on pyrolysis should open up as shown in Chart II to give the desired C_{14}-ketone.

With this in view, mixtures of (+)-limonene (0.1 mol) and methyl vinyl ketone (0.1 to 0.2 mol) dissolved in solvents such as acetic acid, ethanol and hexane were

irradiated using a 125-watt Hanovia medium pressure mercury lamp at temperatures in the range of 15°C to 35°C and for periods ranging from 4 to 16 hours. In all these cases, (+)-limonene was recovered unchanged and methyl vinyl ketone got polymerised (Table I) and therefore this route was not further pursued.

Table I: Photochemical Cycloaddition* of (+)-Limonene with MVK

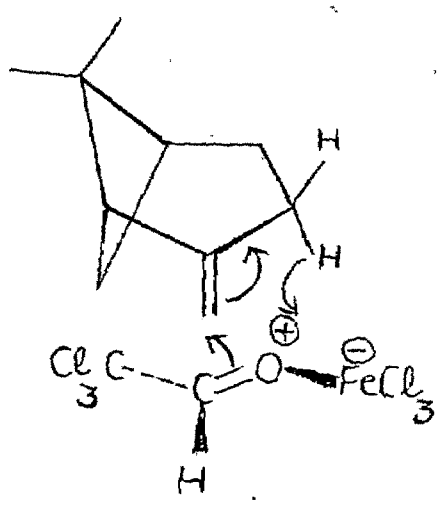
Expt. No.	Limonene (g)	M.V.K (g)	Solvent	Vol. of solvent (ml)	Filter	Temp. °C	Time (hrs)	Product
1	13.6	7.0	AcOH	250	Quartz	30	16	limonene
2	"	"	"	"	"	35	8	11.0 g "
3	"	14.0	"	"	"	20	4	12.1 "
4	"	7.0	EtOH	100	"	15	8	12.0 "
5	"	"	"	"	Pyrex	15	8	12.5 "
6	"	"	Hexane	"	Quartz	15	4	polymer

* Hanovia medium pressure mercury lamp, 125 watt. For other details, see Experimental.

ii) Ene Reaction

The 'ene reaction' is closely related to [2 + 4] cycloadditions of the Diels-Alder type in which a C-H σ-bond plays the role corresponding to one of the diene double bonds in the Diels-Alder reaction.[17,18] Generally, the ene reaction is carried out at temperatures of 160°C or above. However, Lewis acid catalysis of the ene reaction allows the reaction to be performed under mild and synthetically useful conditions.

a) Lewis acid catalysed ene reaction: One of the best studied reactions of this type is that of (-)-β-pinene with various enophiles giving excellent yields (70%) of the cycloadducts. The reaction of β-pinene with chloral in presence of ferric chloride is believed to proceed through the least crowded concerted transition state depicted below[19].



Ene reaction of (+)-limonene with excess (2 moles) methyl vinyl ketone in presence of stoichiometric amounts of aluminium chloride always resulted in excessive polymerisation. When the quantity of the Lewis acid catalyst was reduced, the formation of C_{14} ketone was observed. However, the isolated yield was very poor (3.9%). Details are given in Table II.

Table II : Lewis Acid Catalysed Ene Reaction

Expt. No.	Limonene (g)	M.V.K. (g)	Catalyst	Wt. of catalyst (g)	Temp (^oC)	Time (hrs)	Product
1	1.5	1.5	$AlCl_3$	1.40	20	12	2.6g: polymer
2	1.5	1.5	"	"	15	"	3.0g "
3	"	"	"	0.28	"	"	2.5g; viscous liquid*
4	"	"	"	0.14	"	"	1.14g; limonene
5	"	"	$ZnBr_2$	0.90	20	"	
					30	"	0.82g; limonene

* This product, on chromatography over a column of silica gel gave the C_{14} ketone 20 (0.105 g; 3.9%).

b) Thermal ene reaction: Thermal ene reaction possesses wide scope and applicability ranging from industrial to biosynthetic processes[17]. Methyl heptenone, an important intermediate in the perfumery and flavour industry, is manufactured by the ene reaction of isobutene with methyl vinyl ketone formed *in situ* from paraformaldehyde and acetone.[20]

The desired C_{14} ketone 20 could finally be prepared by the thermal ene reaction of (+)-limonene with methyl vinyl ketone by, more or less, following the procedure used for the preparation of methyl heptenone. (+)-Limonene, paraformaldehyde and excess acetone were allowed to react in a rocking autoclave at 275°C under nitrogen atmosphere (1400 psi) for 6 hrs. The crude product was freed from unchanged limonene by a preliminary rough fractional distillation. The total ketonic fractions thus obtained was refractionated using an annular teflon spinning band column (efficiency: about 80 theoretical plates) to give a GLC-pure (10% SE-30, 180°C) fraction. Further chromatographic purification of this fraction over 15% silver nitrate-impregnated silica gel gave essentially the pure ketone 20 and a small amount of isomeric ketone 22.

The major compound analysed for $C_{14}H_{22}O$ (M^+, m/e 206) and was proved to be the desired intermediate 20 on the following basis: Its IR spectrum (Fig: IV-1) showed absorptions at 1720 and 1360 cm^{-1} (methyl ketone) and at 3070, 1640 and 890 cm^{-1} ($\geq C=CH_2$). In its PMR spectrum (Fig: IV-2) a singlet at 2.03 ppm (3H) is attributed to the protons of $\underline{CH_3}CO$ group and a triplet centered at 2.35 ppm (2H) corresponds to the methylene protons next to carbonyl group ($-CH_2-\underline{CH_2}-C=O$). A multiplet centered at 4.71 ppm (2H) is attributable to protons on an olefinic methylene group. A broad singlet at 5.34 ppm (1H) and a singlet at 1.62 ppm (3H) corresponds to $\underline{CH_3}-C=\underline{CH}$ group. Its mass spectral fragmentation pattern (Chart IV) also supported the structural assignment.

The minor compound also analysed for $C_{14}H_{22}O$ (M^+, m/e; 206) and was found to be the isomeric ketone 22 on the following evidence. The presence of a methyl ketone group was shown by its absorption in the region (Fig: IV-3) at 1720, 1360 and 1160 cm^{-1} and by the presence, in its PMR spectrum, of a 3H singlet at 2.03 ppm. Its PMR spectrum (Fig: IV-4) also showed a triplet (1H, J: 6 Hz) centered at 5.05 ppm corresponding to $CH_3-C=\underline{CH}-CH_2$ of the side chain and a broad singlet at 5.31 ppm (1H) corresponding to $CH_3-C=\underline{CH}-CH_2$ of the cyclohexane ring. A singlet at 1.60 ppm (6H) showed the presence of two methyls

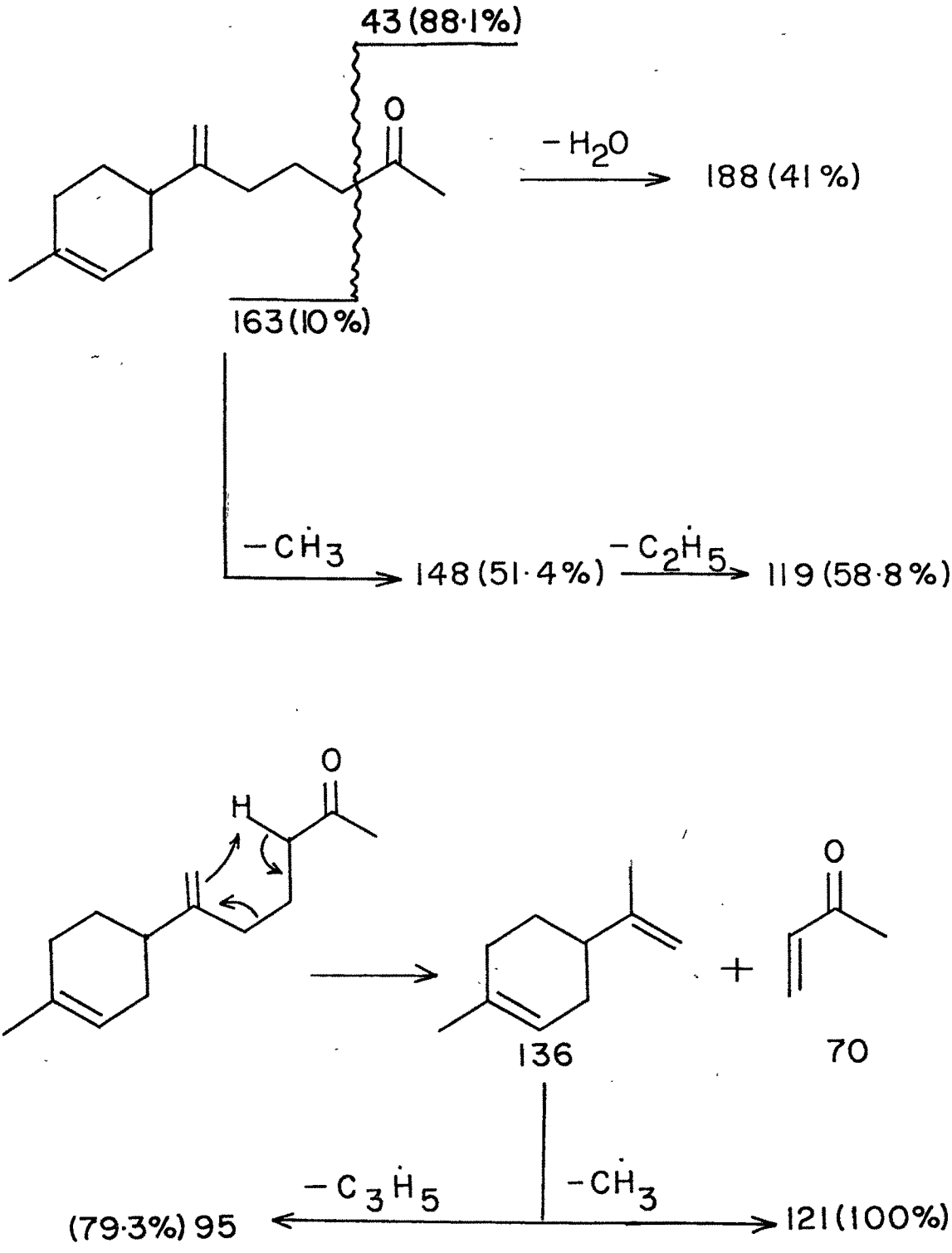
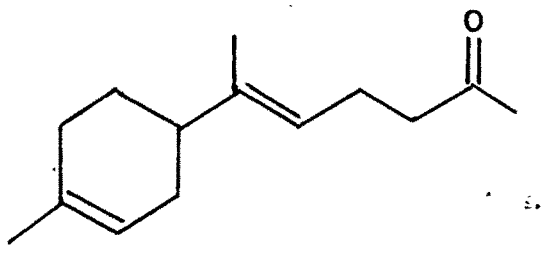


Chart IV: Mass spectral Fragmentation Pattern of The C_{14} – Ketone (20)



(22)

on olefinic linkages.

Synthesis of C_{16}-ester

The ease and superiority of the Emmons-Wadsworth modification of the Wittig reaction over older methods has resulted in its use in the syntheses of numerous compounds.[21]

The C_{14}-ketone (20) on treatment with sodium hydride and dimethyl phosphonoacetate in diglyme/THF at 15°C followed by work-up gave the Wittig product 21 having E-geometry at the newly created double bond (yield 51%).

The pure compound 21 showed in its IR spectrum (Fig: IV-5), bands at 1640, 890 cm^{-1} ($>C = CH_2$) and at 1715, 1635, 1220 and 1150 cm^{-1} ($>=<_{COOMe}$). The following structural features were evident from its PMR spectrum (Fig: IV-6).

CH_3-C=C<u>H</u> (5.60 ppm, 1H, d, J : 1Hz); CH_3-C=C<u>H</u> (5.34 ppm, 1H, bs); C=CH_2 (4.73 ppm, 2H, d, J : 3 Hz); -COO<u>CH_3</u> (3.62 ppm; 3H, s); <u>CH_3</u>-C=C (1.62 ppm, 3H, s). That the newly created double bond is having E-geometry was established by the observation that the methyl group on this double bond is deshielded down to 2.13 ppm (3H, d, J: 1 Hz) due to its being on the same side as the carbomethoxy group.

Selective epoxidation of the C_{16}-Ester

Selective epoxidation of the C_{16}-ester (<u>21</u>) at the cyclohexane double bond could be carried out by the use of perbenzoic acid in benzene at 0^oC. The product consisted of a mixture of epimeric epoxides (α-, and β-), (<u>16</u>).

Compound <u>16</u> analysed for $C_{17}H_{26}O_3$ (M^+, m/e : 278) and absorbed in the IR region (Fig: IV-7) at 1720, 1635, 1235 and 1160 cm^{-1} (>C=CH-$COOCH_3$) and at 1645 and 898 cm^{-1} (>C=CH_2). Its PMR spectrum (Fig: IV-8) showed it to be a mixture of epimeric epoxides with signals at 5.50 (1H, bs, -C<u>H</u>$COOCH_3$), 2.13 (3H, s, <u>CH_3</u>-C=CH-$COOCH_3$ and at 1.25 ppm

(3H, s, CH_3-C(O)-C-) being paired with signals of almost equal height within 0.02 ppm. The two olefinic methylene protons appeared as a broad singlet at 4.72 ppm and the three carbomethoxy protons appeared as a sharp singlet at 3.62 ppm. The proton on the epoxide ring appeared as a multiplet centered at 2.84 ppm.

Juvenile Hormone activity

The JH-activity of methyl cis-10,11-epoxy-8,13-cyclo-7-methylene-3,11-dimethyl-tridec-2(E)-enoate (16) was tested on 4-hr old last instar nymphs of Dysdercus koenigii and the results are given in Table III. The synthesised compound was found to be about ten times more active than farnesyl methyl ether which was used as the standard.

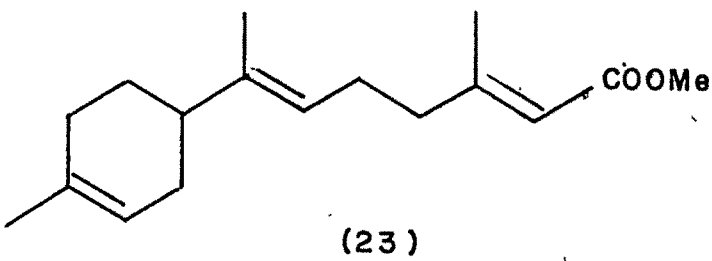
Table III : JH activity of compound 16

No.	Compound	Dose in ug 10.0	1.0	0.1
		Score*		
1	Farnesyl methyl ether	2.0	0.0	0.0
2.	Compound 16	4.0	2.0	0.0

* Score represents mean of two experiments each of which was carried out using three replicates of 15 nymphs each. Nymphs which successfully moulted were characterised and scored as normal adults (0), adult nymphs (1), intermediates (2), nymphs adults (3) and the sixth instar nymphs.

Note

While this work was completed, a report appeared[22] on the syntheses of two related compounds (by a different route) (23) and (24) both of which possess JH activity.



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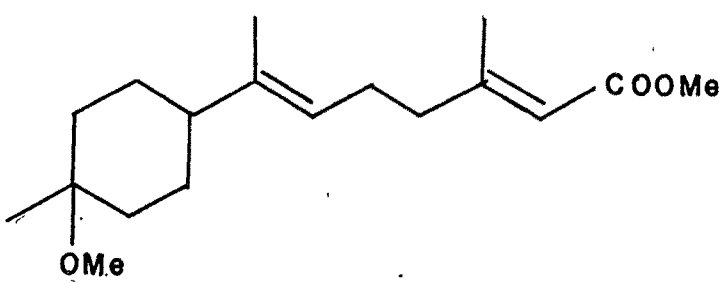

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EXPERIMENTAL

For general remarks, see Chapter II.

Photoaddition of limonene with methyl vinyl ketone

The photoadditions were carried out in a doubly surfaced water cooled glass vessel in specified solvents (Table I). The irradiation was carried out by using a 125 watt Hanovia medium pressure mercury lamp. Samples were taken out (5 ml) at regular intervals. They were worked up by diluting with water and extracting with ether (3 x 10 ml). The organics were washed with 5% bicarbonate (3 x 10 ml), water (4 x 25 ml) and brine (2 x 25 ml). Drying and removal of solvent gave the residues which were analysed by GLC (20% SE-30, 6', 180°C, 60 ml. H_2 flow).

Lewis acid catalised ene reactions

The procedure used is illustrated in the following two examples.

(1) Aluminum chloride: To a magnetically stirred solution of limonene (1.5 gms; 21.4 mmol) in dry benzene (12 ml) was slowly added anhydrous $AlCl_3$ (1.4 gms; 10.5 mmol)

under a nitrogen blanket over a period of 1 hr at 20°C. Vigorous stirring was continued at 20°C for 12 hrs after which the reaction mixture was poured into iced sod. bicarbonate solution. Extraction with ether (25 x 3 ml), brine wash (1 x 50 ml) and removal of solvent furnished a dark residue (2.8 gms) which was chromatographed over silica gel (60 gms).

Chromatogram -I

Col: 2 x 60 cm

SiO_2; (IIA) : 60 gms

Material charged 2.5 gms

S. No.	Solvent	Fraction	Product
1	Pet. ether	4 x 50 ml	0.7912 g (limonene)
2	5% pet. ether/ benzene	6 x 50 ml	0.1050 g (C_{14} ketone
3	Benzene	5 x 50 ml	1.1245 g
4	Ethyl acetate	1 x 100 ml	
		Total	2.0207 g

(2) Zinc bromide: To a well stirred solution of anhydrous zinc bromide (0.9 gms; 4 mmole) in 25 ml of ether (sodium dried) was added limonene (1.5 gms, 11 mmole) and methyl vinyl ketone (1.5 gms; 21 mmole). The resulting mixture was stirred at 20°C for 12 hrs. TLC (benzene) revealed that no reaction had taken place. The mixture was further stirred at room temperature (30°C) for 12 hrs. Still no reaction ensured. The mixture was next stirred at reflux for additional 12 hrs. and the reaction product poured in chilled water (12 ml). The organic layer was separated and the aqueous layer extracted with ether (3 x 25 ml). The organics were washed with brine and dried. Removal of solvent gave the product (0.8240 gms) found to constitute essentially limonene.

Thermal ene reaction

Limonene (27.2 gms; 0.2 mole), paraformaldehyde (12 gms; 0.4 mole), acetone (50 ml) were charged in a rocking type autoclave (Parr Model 4001) under nitrogen pressure (1450 psi) and the mixture was rocked at 275°C for 6 hrs. The contents were cooled and the total crude product (42.1 gms) was distilled using a vigreux column (6") and 4 fractions (total weight: 22.44 gm) were collected

leaving a thick viscous residue (18.01 gms). The distillate composition was checked by GLC SE-30 (10%) on chromosorb W (60-80), 6 ft, 180°C, 60 ml/min H_2 flow.

Table IV : Distillation of crude ene fraction

S.No.	Bpt.	Pressure	Wt./gms	Limonene		Intermediate		C_{14} - ketone	
				%	Wt/gms	%	Wt.	%	Wt.
1.	83-88°C	33 mm	9.4584	100	9.4584	-	-	-	-
2.	88-90°C	33-16 mm	3.3746	97.1	3.2789	2.83	0.0956	-	-
3.	90-98°C	1 mm	7.4186	21.5	1.6010	26.4	1.9613	51	3.8560
4.	98-120°C	1 mm	2.1932	-	-	62.0	1.3609	37.9	0.8322
			22.4448		14.3383		3.4178		4.6882

Yield of ketonic fractions: 24.2% based on consumed limonene.

Refractionation of ketonic fractions

The C-14 ketonic fractions (58.2156 gms) from a few batches were mixed and fractionated on a Perkin-Elmer annular teflon spinning band column (model NFT-51: 80 theoritical plates) at 2 mm pressure.

Table V : Refractionation of ene product

Fraction	Wt/gms	B.p. (^{o}C)	Reflux ratio
1	6.2382	52-80	1:5
2	5.8654	90	1:5
3	3.1343	90-97	1:5
4	3.7563	97-98	1:10
5	1.3764	98	1:20
6	1.2071	98-99	1:20
7	1.7973	99-100	1:20
8	0.0862	100	1:20
9	0.7525	100-101	1:20
10	6.6362	101	1:20
11	2.4380	101-108	1:20
12	2.0255	108	1:20
13	1.3539	108	1:20
14	3.6380	108-112	1:20
Total	40.3023	Residue	13.3753

Fr. 6-10 were found to be a mixture of isomeric C_{14}-ketones.

Chromatography of C-14 ketonic fractions

Chromatogram - II

Column: 3.5 x 56 cm

Absorbent: SiO_2 (15% $AgNO_3$-impregnated)

Material charged: 5.8 gms

Fr.	Eluent	Volume (ml)	Wt/gms
1	Pet. ether	200 x 15	-
2	Pet.ether/ benzene (1:1)	200 x 5	-
3	"	200 x 10	0.7120
4	Benzene	200 x 2	0.1142
5	"	200 x 3	0.7548
6	"	200 x 4	0.6363
7	"	200 x 6	0.6960
8	50% EtOAc/benzene	200 x 13	1.8826
9	"	200 x 2	0.4984
	Total		5.2943 gms

Fr. 5 was distilled at 100-101°C/3 mm to give the C_{14}-ketone (22) n_D^{25} 1.4876 λ_{max}^{EtOH} 210 nm (ε = 2689)

Mass: m/e 206 (19.5%); 95 (100%), 119 (34.7%), 93 (20.6%); 119 (19.5%); 79, 138 (18.4%); 132 (17.3%); 81 (16.3%); 96 (15.2%); 80 (13%); 123 (11.9%); 55, 105 (11.7%); 67, 91, 188 (10.8%); 14P (8.6%).

(Found: C, 81.09; H, 10.39. $C_{14}H_{22}O$, requires C, 81.55; H, 10.67).

Fr. 7, 8 were found as the pure ketone (20). Fr. 8 was distilled (100-101°C/3 mm) to give 1.6093 gms of ketone 20; n_D^{25}, 1.4853; λ_{max}^{EtOH} 210 nm (ε= 2612)

Mass: 206 (41.1%); 121 (100%); 95 (79.3%); 93 (77.8%); 132 (63.2%); 79 (53%); 148 (51.4%); 105, 188 (41.1%); 173 (23.5%); 85 (14.7%).
(Found: C, 81.11; H, 10.32. $C_{14}H_{22}O$; requires C, 81.55; H, 10.67).

Conversion of C_{14}-ketone to the α-β-unsaturated ester 21

Dimethylphosphono acetate (0.637 g; 0.0035 mole) was added with stirring to a suspension of sodium hydride (0.18g; 50%, dispersion, 0.004 mole; washed free of oil with dry hexane) in diglyme under nitrogen blanket at 15°C. The mixture was stirred at this temperature for 1 hr. To

the resultant thick white mass at 10°C was added C_{14}-ketone (20; 0.618 gms, 0.003 mole) in dry THF (5 ml) and the mixture was stirred at room temperature (28°C) for 20 hrs. followed by 1 hr at 60°C. The mixture was poured into ice-cold water (50 ml) and extracted with ether (5 x 25 ml). The organics were washed with water (3 x 25 ml) and brine (2 x 25 ml). Drying and solvent stripping gave the product (0.9211 gms) which was purified by chromatography.

Chromatogram - III

SiO_2; 30 gms (IIIA)

Col ; 1.4 x 44 cm

Fr.	Solvent	Volume	Wt/gms
1	Pet. ether	5 x 50 ml	0.0886
2	"	4 x 50 ml	0.3826
3	"	2 x 50 ml	0.0209
4	"	1 x 50 ml	0.0009
5	Ether	2 x 50 ml	0.4021
		Total	0.8951

Fr. 2 and 3 (0.4035 g, yield 51.3%, homogenous on tlc; 12% ether-pet. ether, R_f 0.49) were mixed and distilled (b.p. 165-170°(bath)/2 mm) to give pure ester 21 λ_{max}^{EtOH} 220 nm (ε= 9938).

Epoxidation of the C_{16}-ester

The ester (21) (0.1642 gms, 0.63 mmole) was cooled to 0°C and perbenzoic acid (0.0953 g, 0.69 mmole) in benzene was added dropwise to it at 0°C. Sod. bicarbonate (0.100 gms) was next added and the contents allowed to stand for 18 hrs. at 5°C with occasional shaking. Cold water (2 ml) was added and the organics were washed with ice-cold 10% NaOH (4 x 20 ml) ; water (5 x 20 ml) and brine (2 x 20 ml). Drying and solvent removal furnished a product (0.1852 gms) which was purified by IDCC[23].

Chromatogram - IV

Col. : 1 x 20 cm
SiO_2: 30 gms
Solvent: 50% ether/pet. ether

Fr.	Wt.	Remarks
1	0.0246 gms	Starting material plus epoxide
2	0.1359 gms	Pure epoxide (R_f 0.47)
3	0.0112 gms	Diepoxide (R_f 0.28)
Total	0.1717 gms	

Fr. 2 (0.1359 gms, yield 78.1%) found homogenous on TLC (R_f 0.47, 50% ether/pet. ether) was distilled at 145-160°(bath)/0.15 mm to give the pure epoxide (15).
λ_{max}^{EtOH} 222 nm (ε= 9304).
$n_D^{25.5}$: 1.4955 . M^+ m/e : 278 (2.6%); 95 (100%); 43, 94 (65%), 93 (41.55%); 67 (39.22%); 79 (36.36%); 81(35.06%); 119 (33.76%); 55 (31.17%); 105, 107, 108 (29.87%); 121 (25.97%); 114 (23.50%); 127 (18.15%); 147 (15.58%).
(Found C, 79.02; H, 9.52; $C_{17}H_{26}O_3$, requires C, 79.38; H, 9.35).

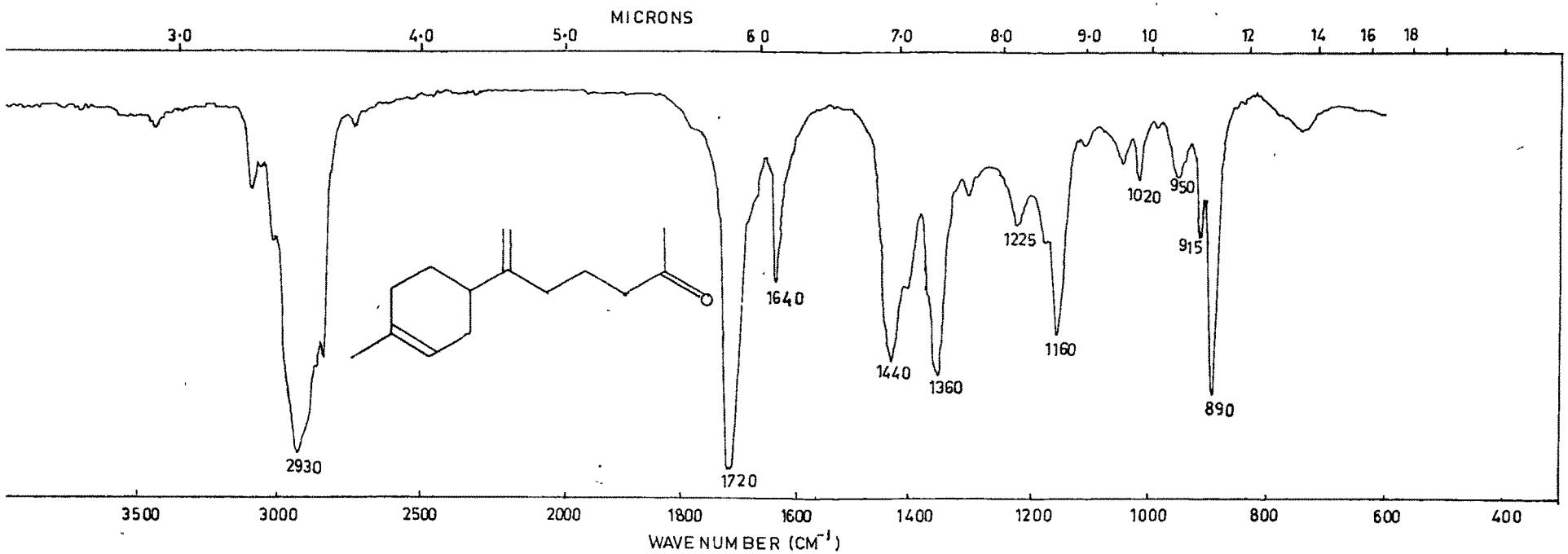

FIG IV-1 : IR SPECTRUM OF C-14 KETONE (20)

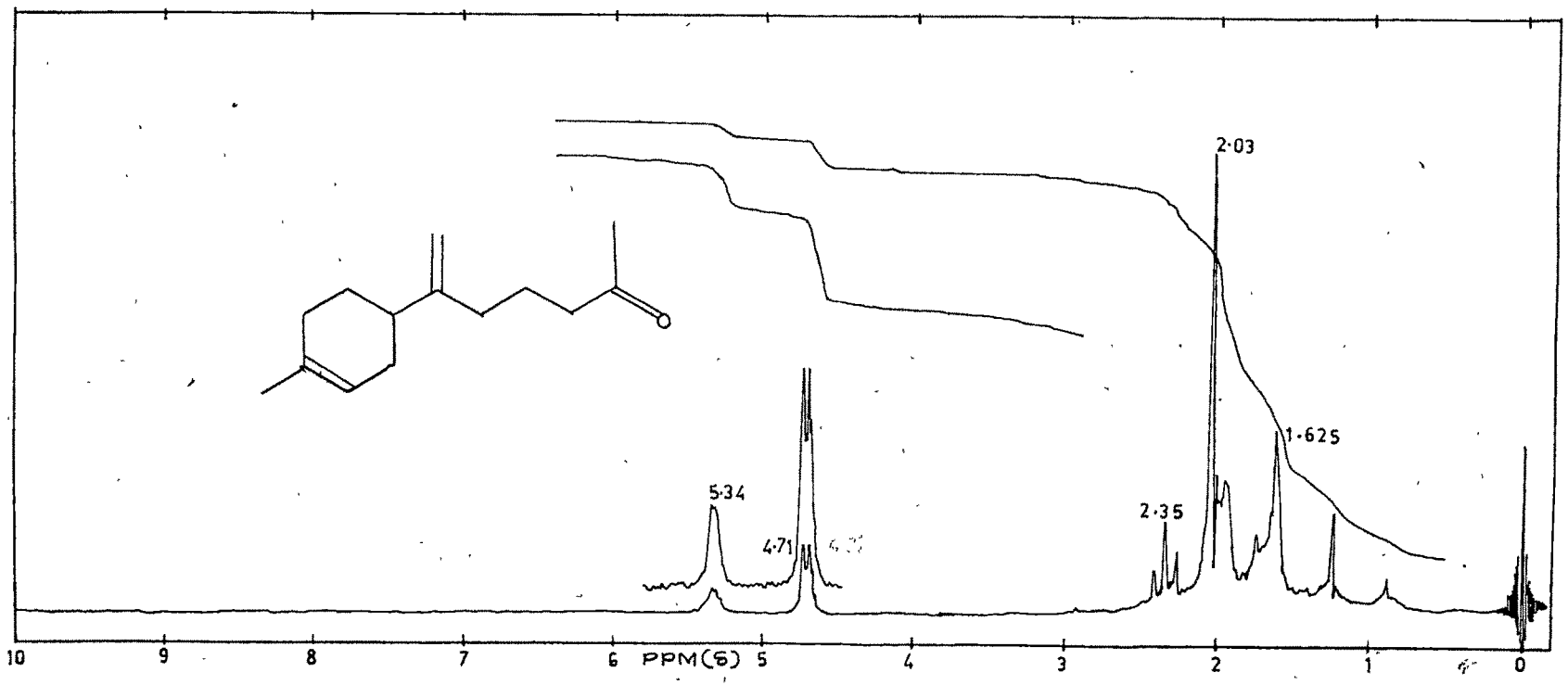

FIG IV-2: PMR SPECTRUM OF C-14 KETONE (20)

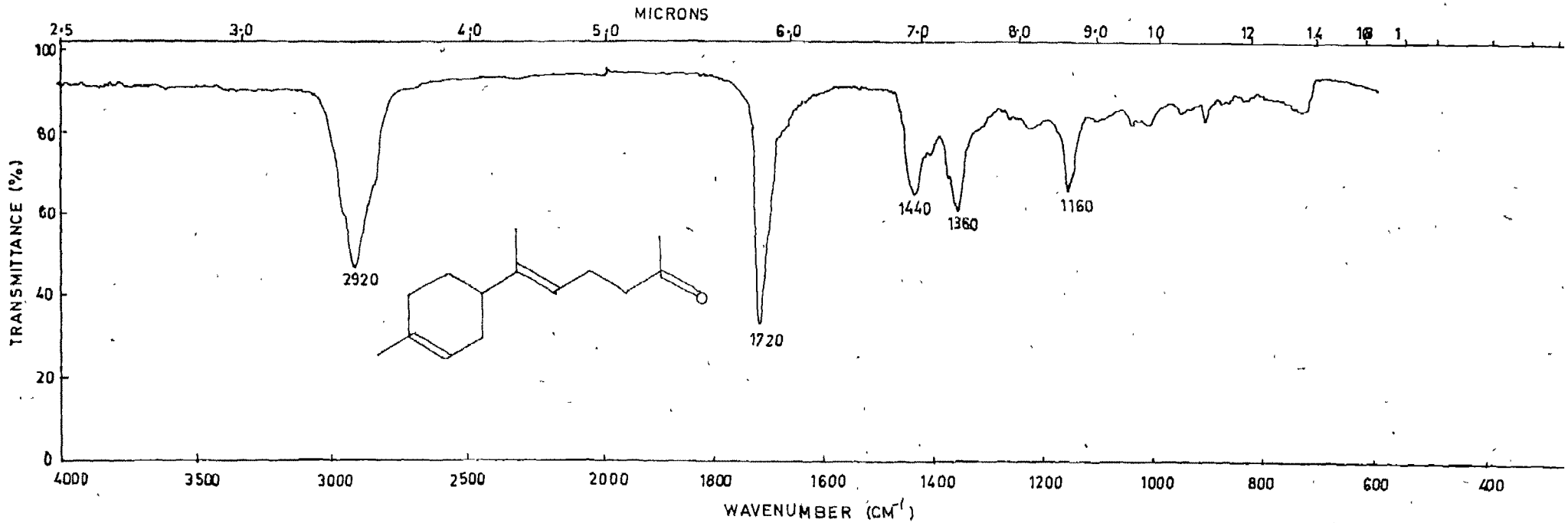

FIG IV-3: IR SPECTRUM OF C-14 KETONE (22)

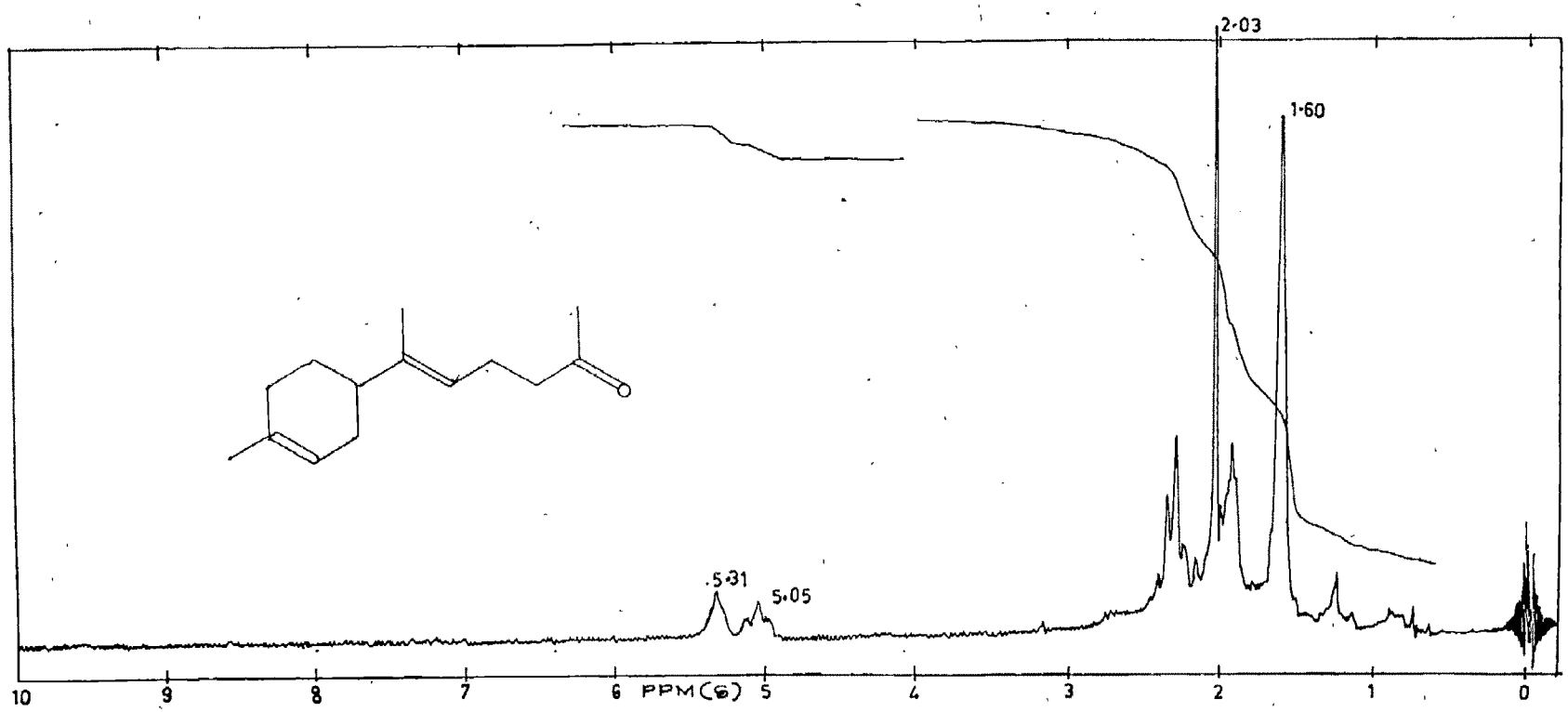

FIG IV-4 : PMR SPECTRUM OF C-14 KETONE (22)

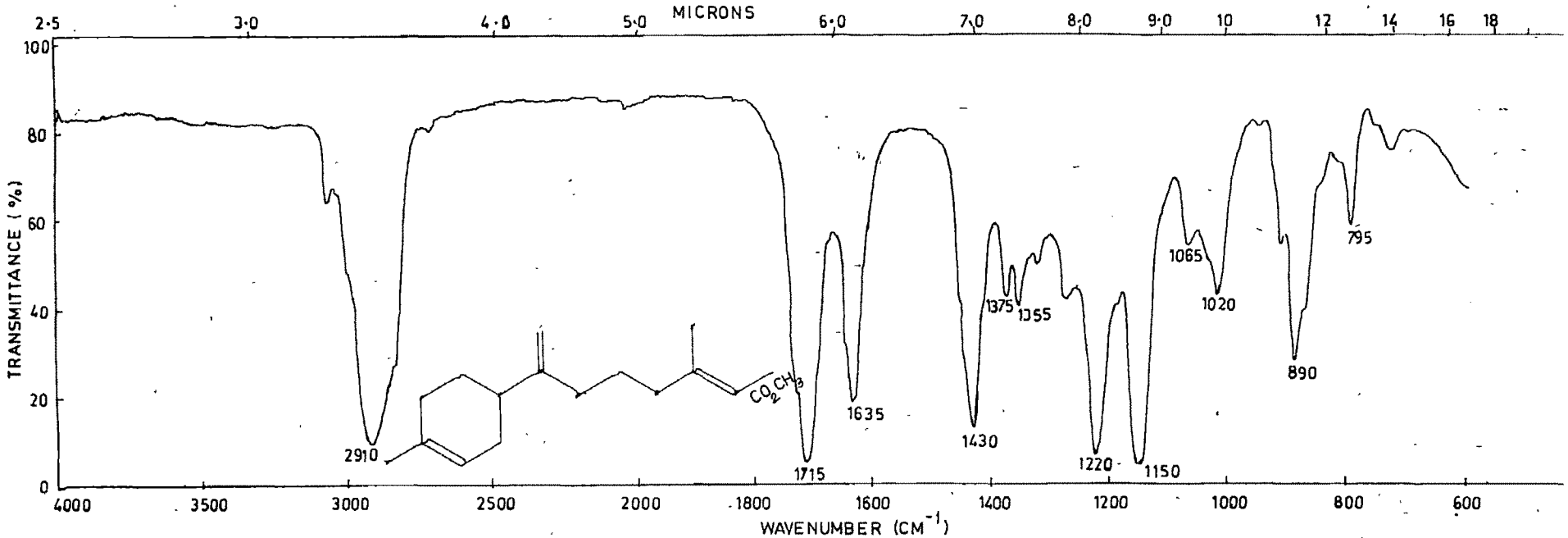

FIG IV-5: IR SPECTRUM OF C-16 ESTER (21)

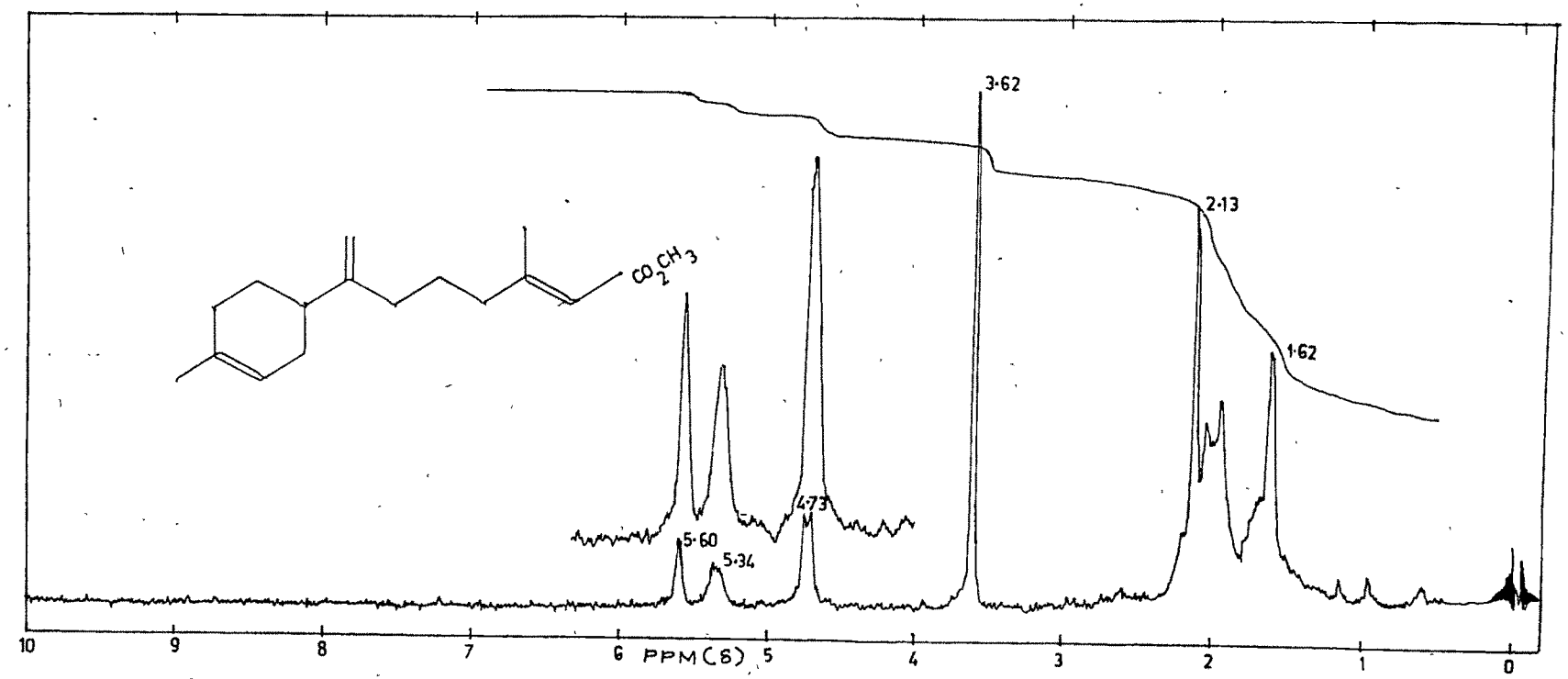

FIG IV-6: PMR SPECTRUM OF C-16 ESTER (21)

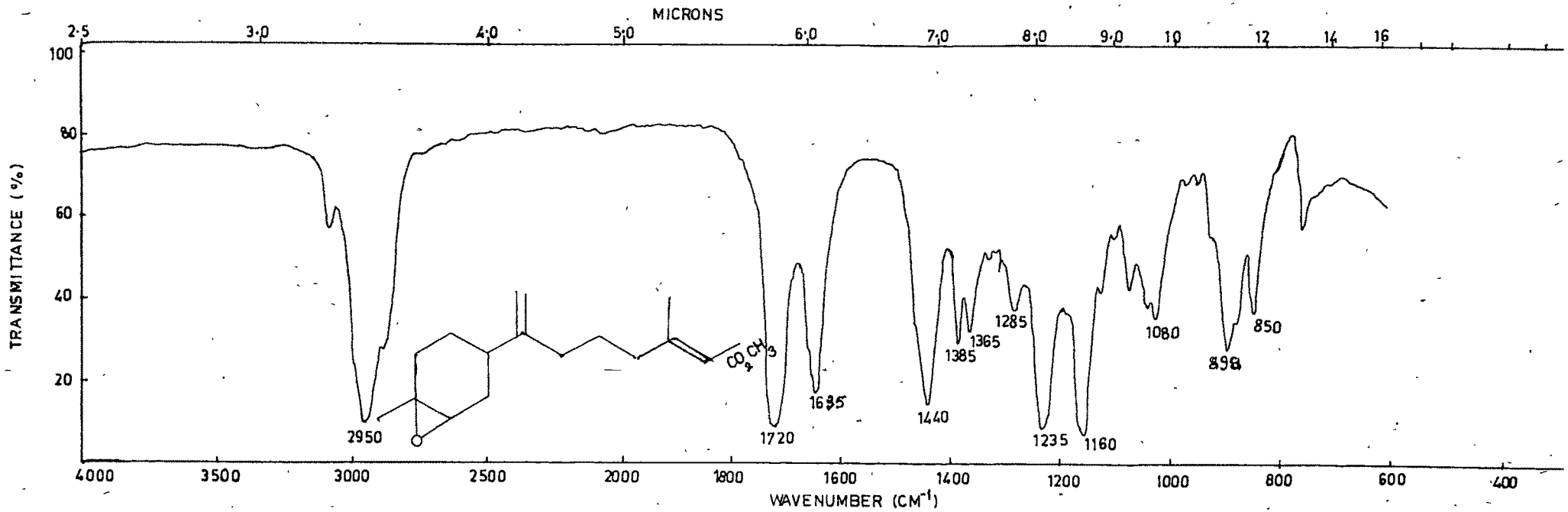

FIG IV-7: IR SPECTRUM OF METHYL CIS-10,11-EPOXY-8,13-CYCLO-7-METHYLENE-3,11-DIMETHYL-TRIDEC-(2E)-ENOATE (16)

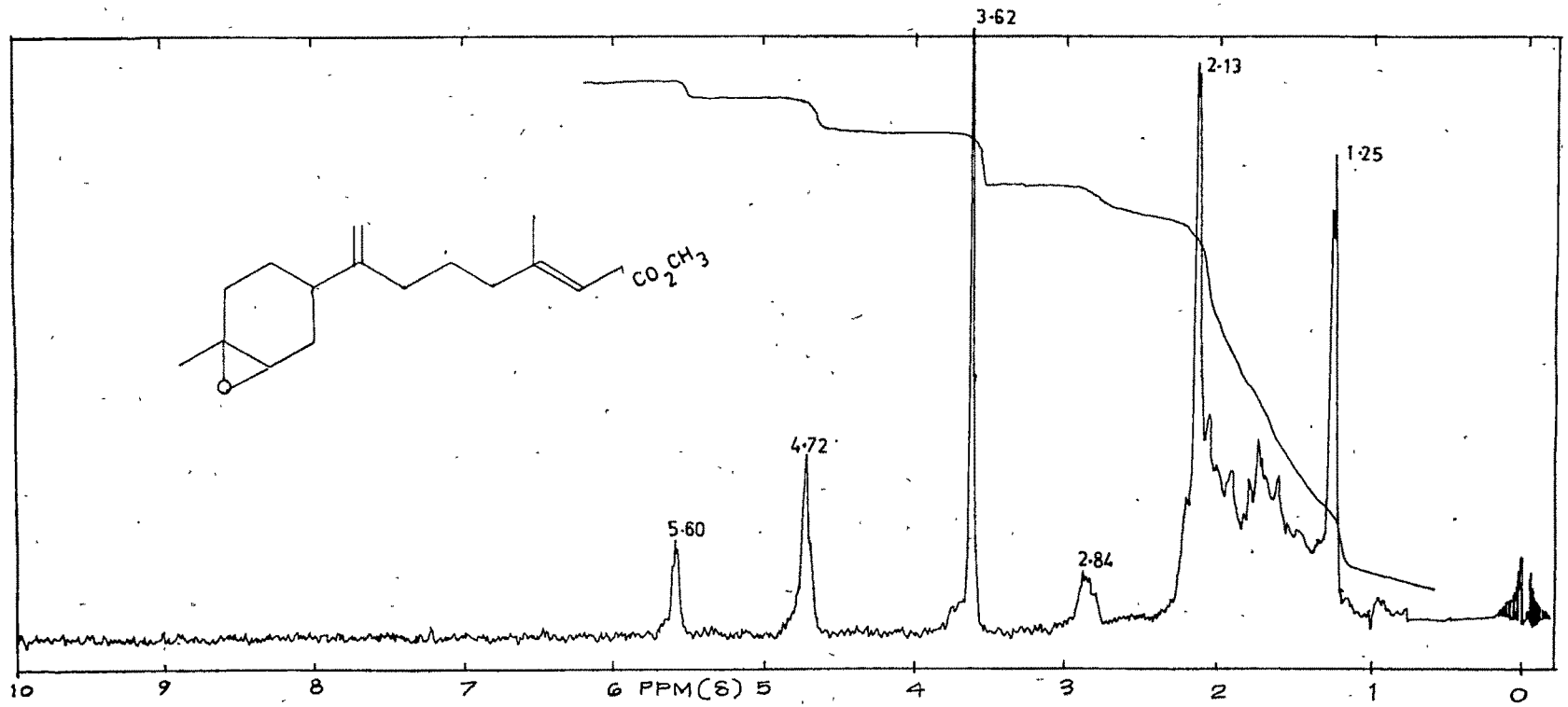

FIG IV-8: PMR SPECTRUM OF METHYL CIS-10,11-EPOXY-8,13-CYCLO-7-METHYLENE-3,11-DIMETHYL-TRIDEC-2(E)-ENOATE (16)

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