CHAPTER-II

SYNTHESIS OF CIS — PERHYDROINDANE AND CYCLONONANE ANALOGUES OF CECROPIA JUVENILE HORMONE

SYNTHESIS OF *cis*-PERHYDROINDANE AND CYCLONONANE ANALOGUES OF *CECROPIA* JUVENILE HORMONE

ABSTRACT

The present Chapter describes the synthesis of *cis*-perhydroindane analogues of *Cecropia* juvenile hormone, from a critical and common starting point — *cis*-bicyclo (4,3,0)nonan-3-8-dione which was prepared from indene; and cyclononane analogue of *Cecropia* juvenile hormone from 5-methyl-cyclonon-4(*Z*)-en-1-one; which was prepared from 2-methyl-cyclo-pentan-1,3-dione.

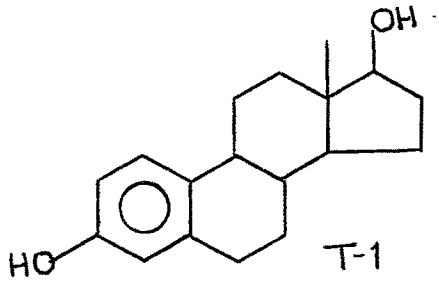
INTRODUCTION

The biological profile of natural products, including their derivatives, and synthetic analogues, served to formulate the early ideas about possible relationship between chemical structure and biological activity. It soon realised that certain structural units of the molecules of biologically active compounds are also to be found in those of other compounds having similar properties. This provided a guiding thought in mapping the structure of further compounds with analogous activities, hopefully more potent, more specific, or less toxic. The molecular modification of a promising "lead" compound is still a major stream of investigation to novel analogues.[1b] Structural changes produce new physical properties, and alter the reactivities of a molecule, which in turn may create changes in distribution in cells, and tissues, in access to active sites of enzymes and receptors, in reaction rates at such sites, and in excretion patterns. Even an apparently very minor variation in chemical structure may thus uncover biological effects that have been dormant or overshadowed by side effects in the parent compound.

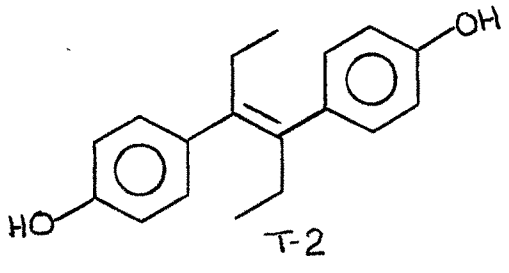
One interesting aspect of molecular modification is the designing compounds, by opening of cyclic or closing of acyclic

Structures[1] which have comparable physical properties and shapes, especially if such features as rigid bonds or intramolecular hydrogen bonds provide an impetus for pseudocyclic conformations.

Among the best known examples are the potent estrogens. The natural estrogenic hormone estrodiol (T-1) can be simulated by the synthetic diethylstilbestrol (T-2). The latter is about



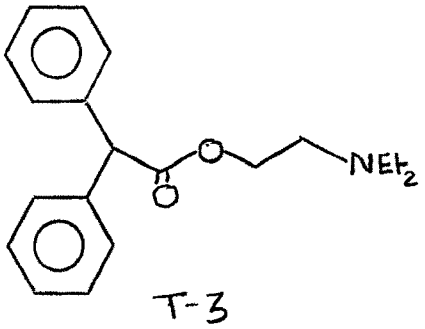
T-1



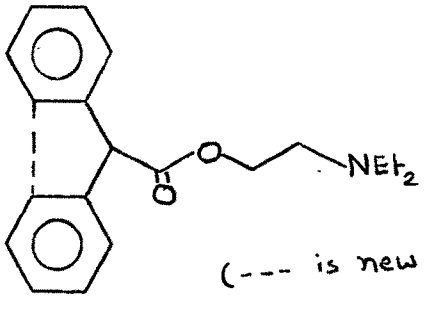
T-2

as active as the natural hormone (T-1), and is much more potent than it's tetracyclic analogue with two terminal phenolic rings.[ac]

In anticholinergic diethylaminoethyl esters, tying back the aromatic rings enhanced the activity[1d,1e] (T-4 is more active than T-3).



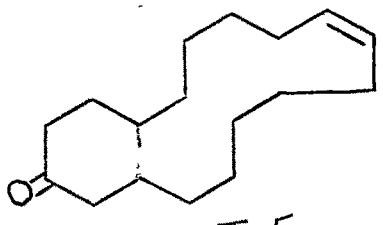
T-3



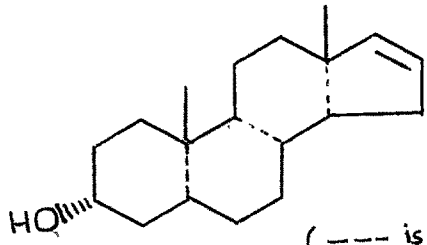
(--- is new bond)

T-4

In the muscone series, the smell of (T-6) is more animal like and closer to natural musk than the purified ring ketones such as civetone (T-5), and muscone which possess a somewhat sweet and flowery note.[1f]

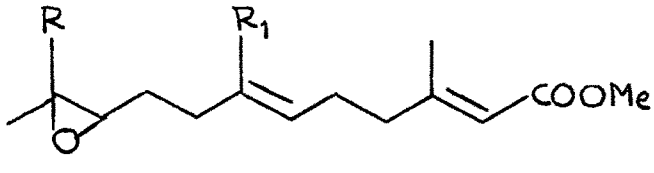


T-5



T-6 (--- is new bond)

This approach to the synthesis of Cecropia juvenile hormones (JH-I, 1; JH-II, 2; JH-III, 3)[2] mimics has not been exploited,



1 : R = R_1 = Et
2 : R = Et, R_1 = Me
3 : R = R_1 = Me

though several analogues with three,[3] four,[4] five,[5,6] and six-membered[5,7,8] rings (Fig. 1) have been reported invariably.

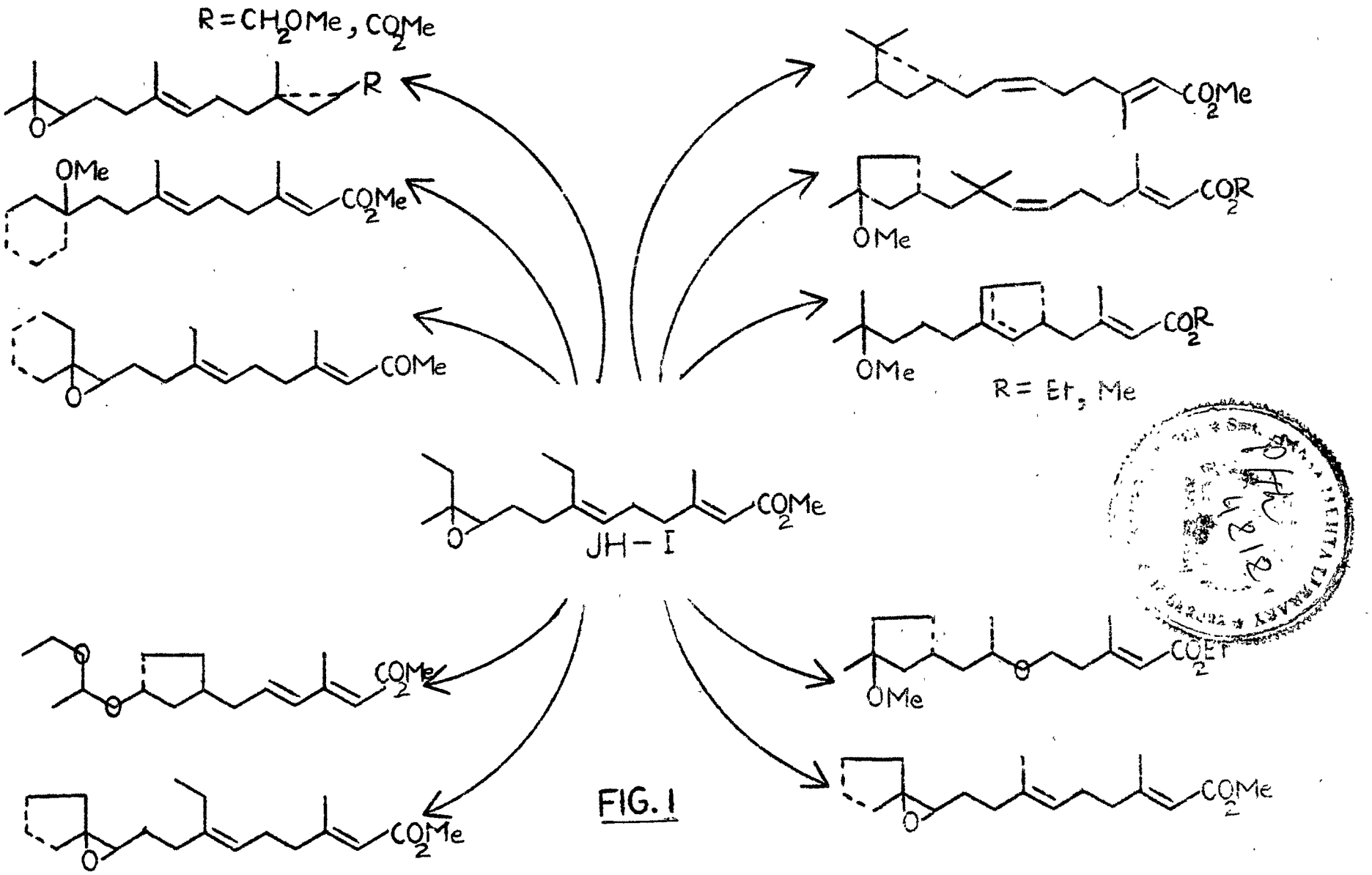

R = CH2OMe, CO2Me
R
OMe
CO2Me
COMe
CO2Me
OMe
CO2R
OMe
CO2R
R = Et, Me
CO2Me
JH - I
COMe
CO2Et
OMe
CO2Me
COMe

FIG. 1

additional carbon atoms have also been incorporated. Many of these compounds were found to be effective growth regulators, though on different insect species. The present investigation was undertaken to see how by closing a part-structure of JH-I (1), the JH-activity would be affected. Of the very large number of structures that can be generated from such an exercise, we have restricted our effort to those schematically shown in Fig. 2. These novel modifications would result in molecules having 2 or 4 hydrogens less than JH-I (1) and having a molecular shape which may be likened to certain frozen conformations of JH-1 (1). Also it is revealed that in going to structures such as 4, 5, 6 and 7 there will be some distortion in the shape of the original molecule (1), but this is not significant as verified from molecular models, the overall essentially linear disposition of the functionality having maintained. The synthesis of 4, 5, 6 and 7 is described in the present chapter, which form the subject matter of subsequent sections.

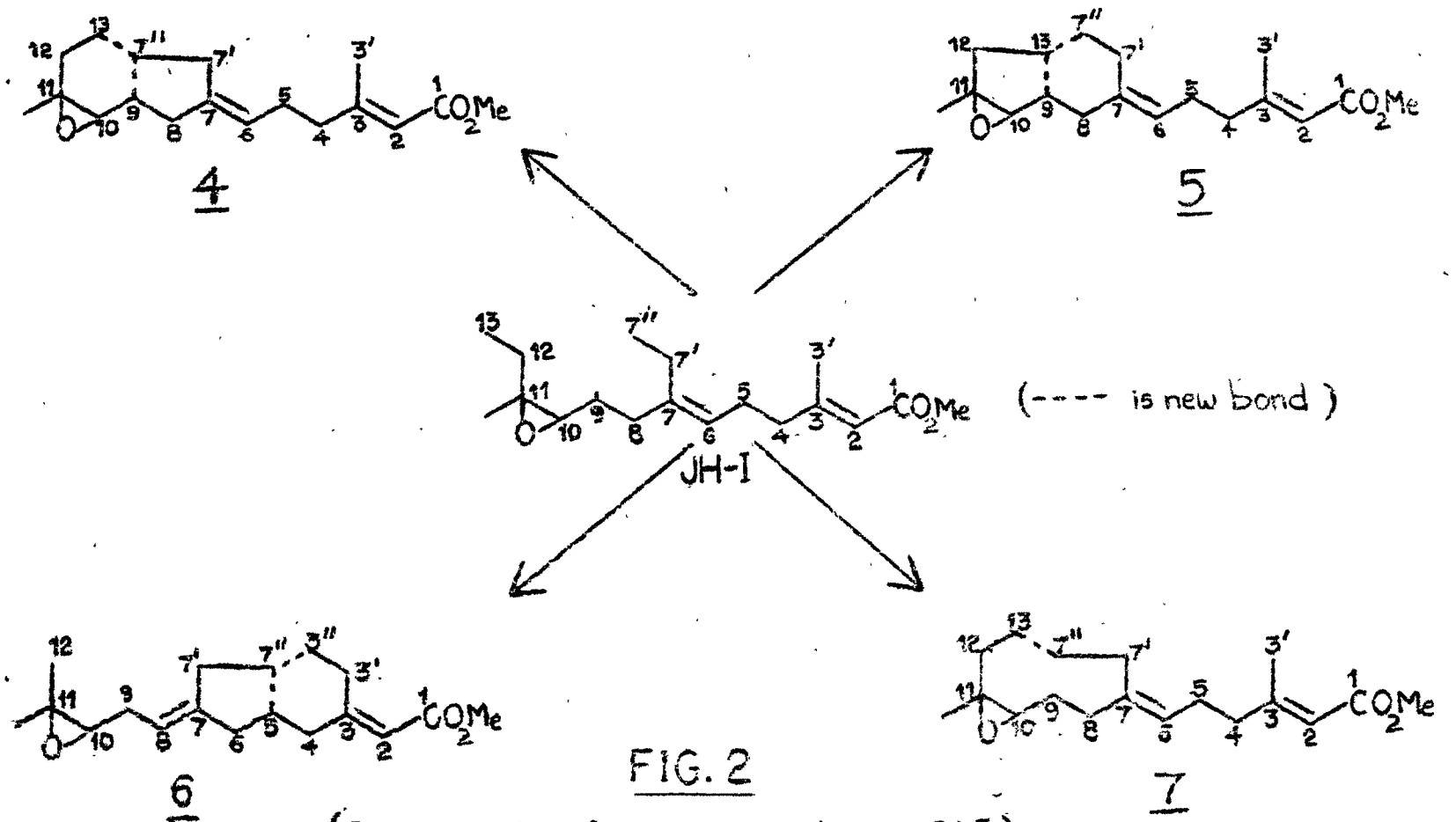


FIG. 2

(Some modes of ring incorporation in JH-I)

SECTION–I

CIS - PERHYDROINDANE ANALOGUES OF CECROPIA JUVENILE HORMONE (Part - I)

dl-Methyl 7" : 9, 7" : 13 - and dl-Methyl 7" : 13, 9 : 13 - cis - cyclo cis - 10, 11 - epoxy - 7 - ethyl - 3, 11 - dimethyl - trans - 2, trans - 6 - tridecadienoate.

cis-PERHYDROINDANE ANALOGUES OF CECROPIA JUVENILE HORMONE (Part I)

INTRODUCTION

The synthesis of dl-methyl 7" : 9, 7" : 13 - and dl-methyl 7" : 13, 9 : 13-cis-cyclo-cis-10, 11-epoxy-7-ethyl-3,11-dimethyl-trans-2, ξ-6-tridecadienoate+; 4 and 5 is described in the present section. Their relation to JH-I (Fig. 2) is interesting in so far as they can be visualized as derived from JH-I ring closures at positions 7" : 9, 7" : 13; and 7" : 13, 9 : 13 respectively.

RESULTS AND DISCUSSIONS

cis-Bicyclo(4,3,0)nonan-3,8-dione

For the synthesis of 4 and 5, cis-bicyclo(4,3,0)nonan-3, 8-dione (10) appeared to be a critical and common starting point. The preparation of 10 has, apparently, not been reported so far. Suitably constructed indan-2,5-diols can be hydrogenated

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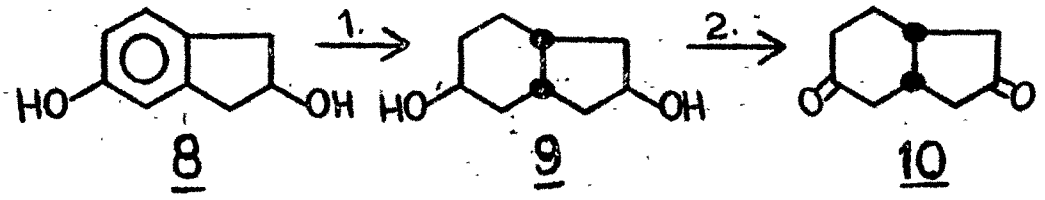
ξ Either E or Z geometry

+ This nomanclature is based on the name of the parent JH-I; 7" : 9, 7" : 13; and 7" : 13, 9 : 13 indicate that these positions are joined together to form perhydroindane ring. Similar nomanclature is well-known in steroid field.

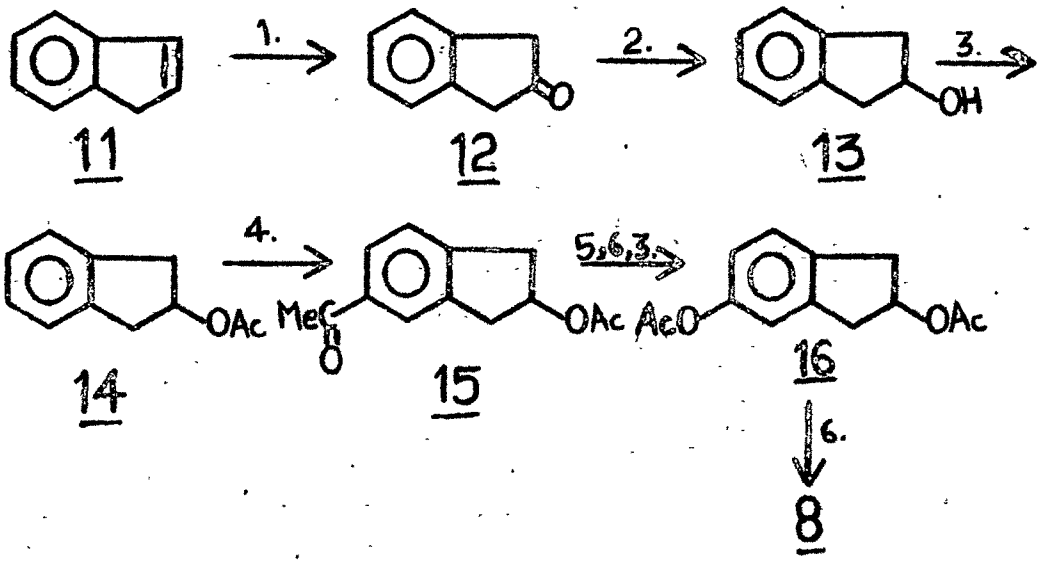
under pressure, in presence of catalyst to yield saturated diol, in which the ring junction between five- and six-membered ring formed is exclusively cis.[9] The diols then can be readily oxidized[10] to diketones. This approach (Fig. 3) appeared most suitable for the synthesis of 10.

The required diol 8 was prepared from indene, along the lines indicated in Fig. 4. Indene 11 was converted to the ketone 12 with $HCOOH/H_2O_2$,[11] diluted H_2SO_4; and thence to the alcohol 13 with LAH/Ether[12] or with $NaBH_4/CH_3OH$. Acetylation of 13 with aceticanhydride-pyridine furnished the acetate 14. The acetate 14 was acylated at C_5 position with $AlCl_3/CH_3COCl$, CS_2[13] to yield the ketone 15. Baeyer-Villiger oxidation[14] of 15 with performic acid produced a mixture of diol formate-acetate which upon alkaline hydrolysis gave a diol which on further acetylation afforded the desired diacetate 16. Refluxing of 15 with KOH in CH_3OH furnished indan-2,5-diol [8; Mass: m/e 150. IR (Fig. 1): (KBr-pellet): OH 3380 cm^{-1}]. High pressure hydrogenation[9] of 8 with Raney Ni, W_2[15]/EtOH in presence of alkali afforded, in excellent yield, the required saturated diol 9; in which the junction of five-and six-membered ring is considered to be cis (9), in view of the known[9] high pressure hydrogenation of hydroxy indanes. Jone's oxidation[10] of 9 furnished the expected cis-bicyclo(4,3,0)nonan-3,8-dione [10; Mass (Fig. 4A): m/e 152. IR (Fig. 3): (CCl_4): five-membered C=O 1755 cm^{-1}, six-membered C=O 1725 cm^{-1}. PMR (Fig. 4): CH, CH_2, 12H, 1.6-3.0 ppm, 6m].



REAGENTS : 1. Raney Ni, W_2 / H_2 / EtOH ; 2: CrO_3 / dil. H_2SO_4 / Acetone

FIG. 3



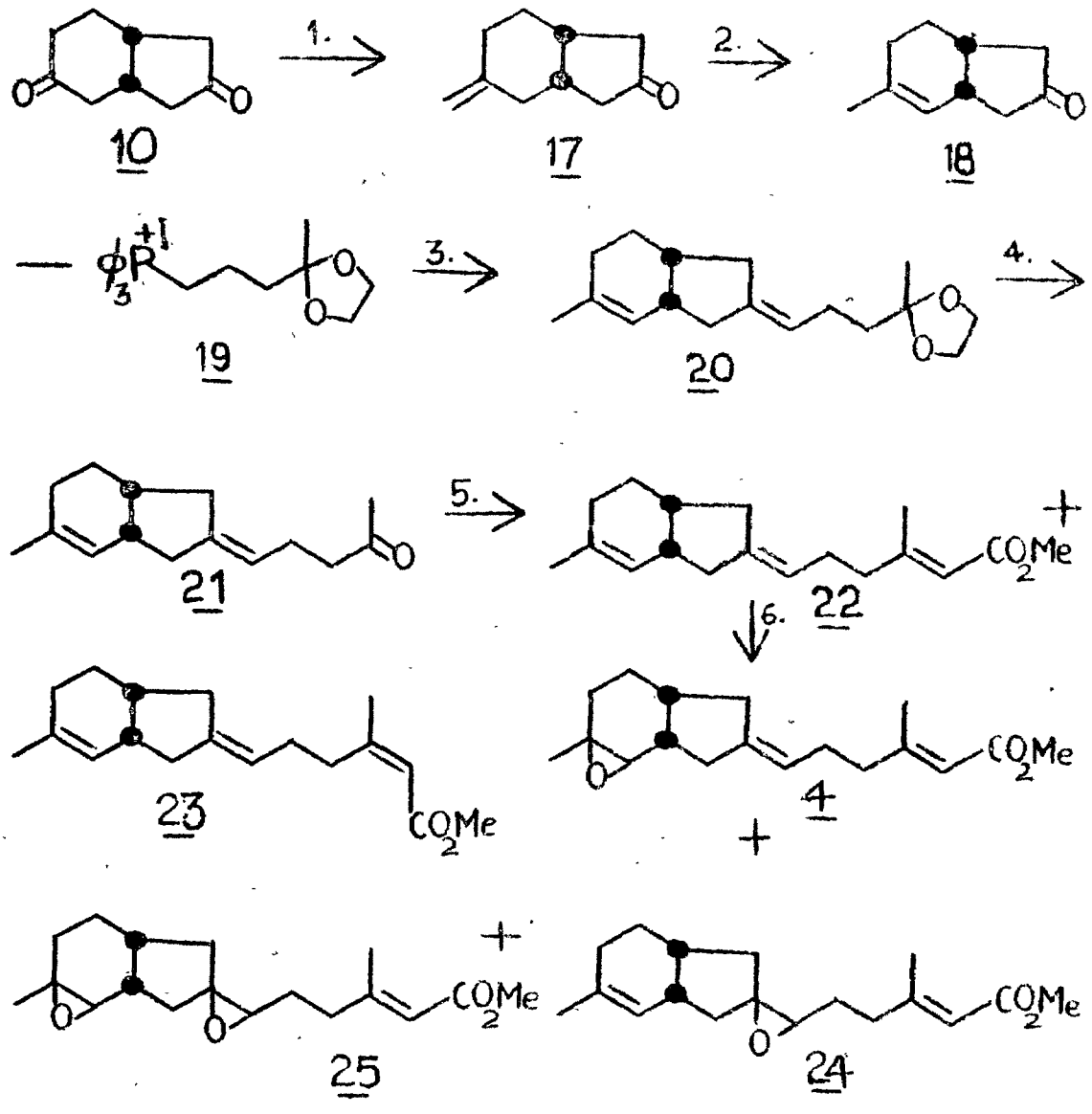
REAGENTS : 1. HCO_3H / dil. H_2SO_4, Steam distillation ; 2. $NaBH_4$ / EtOH ; 3. Ac_2O / Pyridine ; 4. MeCOCl / $AlCl_3$ / CS_2 ; 5. HCO_3H ; 6. NaOH / MeOH

FIG. 4 : Synthesis of indan-2,5-diol

cis-Perhydroindane analogue of JH-I (4)

The synthesis of 4 from 10 was achieved according to the scheme briefly outlined in Fig. 5. The starting diketone 10 was converted to the olefin 17 with methylenetriphenyl phosphorane.[16] Conditions for this selective Wittig reaction at six-membered carbonyl were critical, but the process became efficient when carefully executed (strictly anhydrous conditions, inverse addition[16] of one equivalent of the reagent and temperature in the range of 0-3°). The olefin exhibited spectral characteristics expected of 17 [Mass: m/e 150. IR (Fig. 5): five-membered C=O 1745 cm^{-1}, C=C 1658, 1450 cm^{-1}. PMR (Fig. 6): C=C$\underline{H}_2$, 2H, 4.73 ppm, d, J=6Hz].

Refluxing of 17 with p-toluene sulfonic acid in benzene furnished the desired isomerized olefin [18; Mass: (Fig. 8A): m/e 150. IR (Fig. 7): five-membered C=O 1745 cm^{-1}, C=C 1458, 1442 cm^{-1}. PMR (Fig. 8): Me C=C, 3H, 1.68 ppm, bs; Me C=C$\underline{H}$, 1H, 5.36 ppm, d, J=2Hz]. Wittig reaction of the ketone 18 with the phosphonium salt 19[17] in presence of potassium-t-butoxide/THF afforded the ketal 20 which upon hydrolysis with p-toluene sulfonic acid/acetone furnished the dienoic ketone exhibiting spectral characteristics expected of 21 [Mass: (Fig. 10A): 218. PMR: Me C=C, 3H, 1.65 ppm, bs; CO$\underline{Me}$, 3H, 2.16 ppm, ss; Me C=C$\underline{H}$, C$\underline{H}$=C, 2H, 5.12 ppm, W_H=17Hz; 5.30 ppm, W_H=13Hz, two bm.



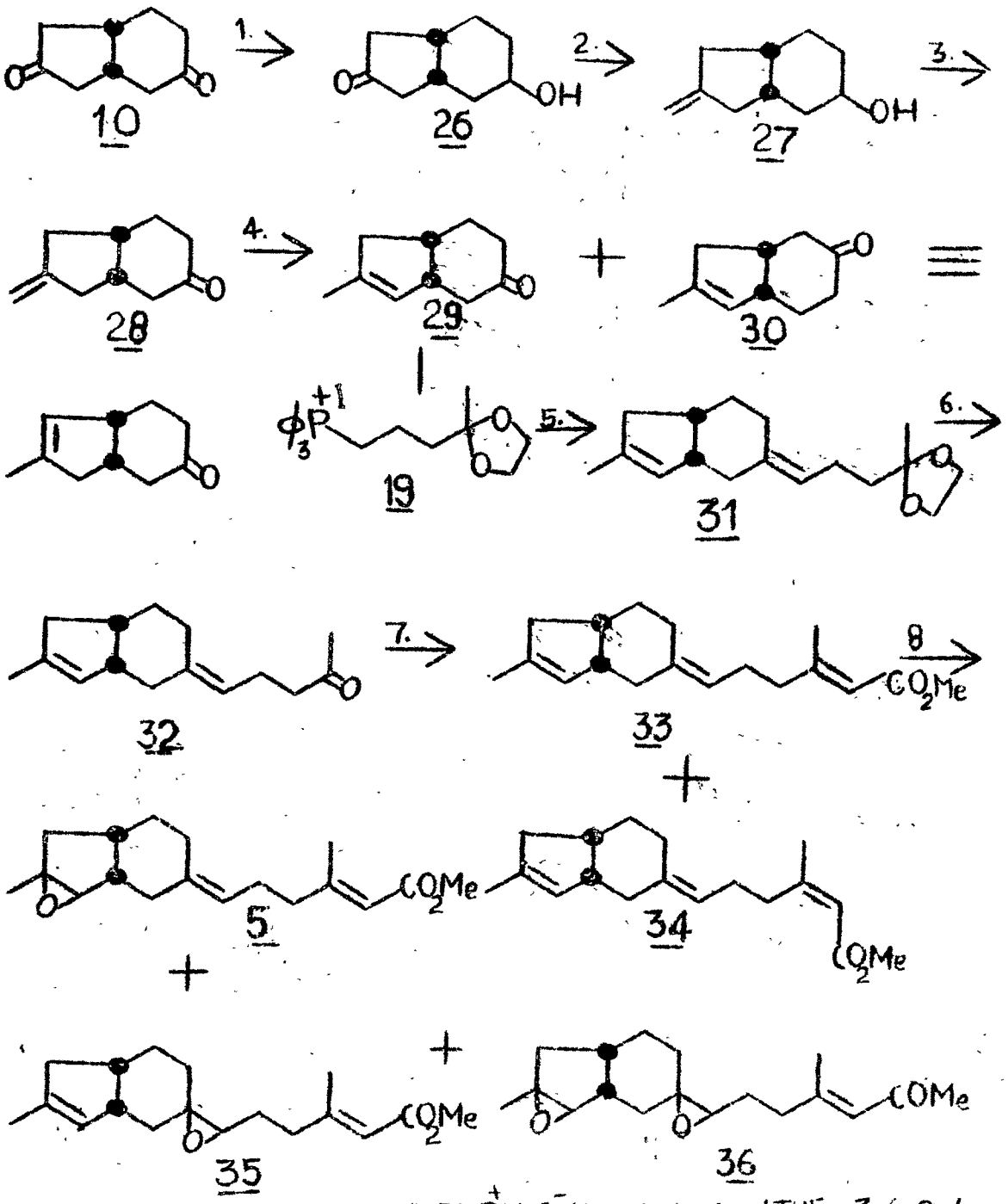
REAGENTS: 1. $Ph_3P^+MeI^-$ / K-t-butoxide / THF ; 2. PTS / C_6H_6 ; 3. K-t-butoxide / THF ; 4. PTS / Acetone ; 5. $(EtO)_2P(O)CH_2CO_2Me$ / NaOMe / DMF ; 6. m-Cl-Ph_3CO_3H / CH_2Cl_2

FIG. 5. Synthesis of cis-perhydroindane analogue of JH-I; 4

Glc: R_f 4.5 min (97%), 5% carbowax 20M, 6', 200°, 60 ml/min ; the (either Z or E) geometry of $\Delta^{5,6}$ double bond remains unsolved from the PMR data or from analysis of similar cases.[17] Condensation of the ketone 21 with methyldiethylphosphonoacetate[18] in the presence of NaOMe/DMF[19] gave rise to a mixture of E - and Z-esters (22 and 23), could readily be separated by inverted-dry-column-chromatography (IDCC)[20], and identified as one would expect different chemical shift in PMR (Fig. 12 and 14) for C_3-Me signals for the E-(22, 2.15 ppm) and Z-isomers (23, 1.88 ppm)[21]. Epoxidation[22] of E-ester 22 with m-Cl-$PhCO_3H$[23]/CH_2Cl_2 at 0° followed by tlc purification afforded the targeted cis-perhydroindane analogue of JH-I in the racemic form [4; Mass (Fig. 16A): m/e 290. IR (Fig. 15): C=O 1720 cm^{-1}, C=C 1648, 1432, 860 cm^{-1}. PMR (Fig. 16): Me.C(—O)—C, 3H, 1.26 ppm, ss; Z-Me.C=C.COOMe, 3H, 2.16 ppm, ss; COOMe, 3H, 3.62 ppm, ss; Me C=C, 3H, 1.66 ppm, bs, is it due to contamination of 24?; CH=C, 1H, 5.10 ppm, m, W_H=14Hz; 5.28 ppm, m, W_H=10 Hz; C=CH COOMe, 1H, 5.58 ppm, bs].

cis-Perhydroindane analogue of JH-I (5)

The synthesis of 5 from 10 was accomplished by the path shown in Fig. 6. The diketone 10 was selectively reduced[24] with $NaBH_4$/EtOH[25] at 0° to produce the anticipated hydroxyketone 26 Mass: m/e 154. IR (Fig. 17): OH 3460 cm^{-1}, five membered C=O 1740 cm^{-1}. PMR: CHOH, 1H, 3.5-4.0 ppm, bm . Action of five-fold excess[26] $Ph_3P^+MeI^-$ on the hydroxy ketone 26, in presence of potassium-t-



REAGENTS: 1. $NaBH_4$ / EtOH ; 2. $Ph_3\overset{+}{P}MeI^-$ / K t-butoxide / THF ; 3. CrO_3 / Pyridine - supported on SiO_2-gel / CH_2Cl_2 ; 4. PTS / C_6H_6 ; 5. K t-butoxide / THF ; 6. PTS / Acetone ; 7. $(MeO)_2P(O)CH_2CO_2Me$ / NaOMe / DMF ; 8. m-Cl-$PhCO_3H$ / CH_2Cl_2

FIG. 6. Synthesis of cis-Perhydroindane analogue of JH-I ; 5

butoxide/THF furnished the expected hydroxy olefin 27 (IR (Fig. 18): OH 3340 cm^{-1}, C=C 1660, 1452 cm^{-1}. PMR (Fig. 19): CH_2=C, 2H, d, 4.83 ppm, J=2Hz). Chromium trioxide-pyridine (supported on silica gel)[27] oxidation of 27 furnished in high yield, the required olefinic ketone 28. Refluxing of 28 with p-toluene sulfonic acid in C_6H_6 yielded a mixture of isomerized olefins (29 and 30), could readily be separated by preparative gas chromatography, and identified by PMR, as one would expect Z-protons (2.8 ppm, d),

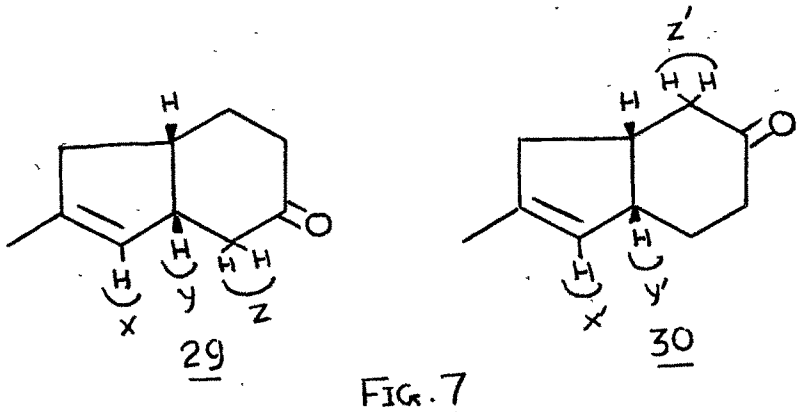


FIG. 7

as singlet on decoupling Y-proton (2.08 ppm, m) which in turn was located by decoupling x proton (5.16 ppm, d) in 29. Similar decoupling experiments did not affect the doublet of Z' protons, as expected in 30 (Fig. 7). The ketone 29 on exposure to (4,4-ethylenedioxy) pentylene triphenylphosphorane[17] in tetrahydrofuran, yielded the desired Wittig ketal 31 which on hydrolysis with p-toluene sulfonic acid-acetone furnished dienoic ketone exhibiting spectral characteristics expected of 32 [Mass (Fig. 27A): m/e 218. IR (Fig. 26): C=O 1730 cm^{-1}, C=C 1450, 868 cm^{-1}. PMR (Fig. 27): Me C=C, 3H, 1.70 ppm, bs;

COMe, 3H, 2.05 ppm, ss; Me C=CH, CH=C, 2H, 5.10 ppm, W_H=21Hz, bm, Glc: R_f 4.96 min (98%), 5% carbowax 20M, 6', 190°, 60 ml/min], the ? (either Z or E) geometry of $\Delta^{5,6}$ double bond remains obscure from the PMR data or from analysis of similar cases.[17] The ketone 32, on interaction with trimethylphosphonoacetate[28] in presence of potassium-t-butoxide/THF, underwent Wittig reaction to furnish a mixture of trienoic E- and Z-esters (33 and 34), could readily be resolved by inverted-dry-column-chromatography (IDCC)[20], and identified, as one would expect different chemical shift in PMR for C_3-Me signal for the E-[33, 2.13 ppm (Fig. 29)] and Z-isomers [34, 1.88 ppm (Fig. 31)][22]. Selective epoxidation[22] of the E-ester 33 with m-Cl-perbenzoic acid[23] in methylenedichloride afforded a mixture of epoxides from which the targeted cis-perhydroindane analogue of JH-I (5) was obtained by preparative-layer-chromatography (PLC). [5; Mass (Fig. 33A): m/e 290. IR (Fig. 32): C=O 1730 cm^{-1}, C=C 1656, 1442, 868 cm^{-1}. PMR (Fig. 33): Me C—C (O), 3H, 1.35 ppm, ss; Z-Me.C=C.COOMe, 3H, 2.16 ppm, bs; COOMe, 3H, 3.62 ppm, ss; Me.C=C, 3H, 1.70 ppm, bs, is it due to contamination of 35?; CH=C, 1H, 5.0 ppm, m, W_H = 21 Hz; C=CH.COOMe, 1H, 5.57 ppm, d, J = 4 Hz].

EXPERIMENTAL

All m.ps and b.ps are uncorrected. Light Petroleum refers to the fraction b.p. 60-80°. All solvent extracts were finally washed with brine and dried (Na_2SO_4).

The following instruments were used for spectral/ analytical data: PerkinElmer, model R-32 (90 MHz) NMR spectrometer; Varian Mat CH-7 Mass spectrometer (70 eV, direct inlet system); Hewlett-Packard 5712A and 7624A gas chromatographs (Al columns, 180 cm x 0.6 cm; support, 60-80 mesh chromosorb W; carrier gas, H_2). All PMR spectra were recorded with 15-20% soln in CCl_4 (unless otherwise stated) with TMS as internal reference, signals are reported in ppm (δ); while citing PMR data the following abbreviations have been used: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad singlet; ss, snarpsinglet; bm, broad multiplet. While summarising mass spectral data, besides the molecular ion, ten most abundant ions (m/e) are reported with their relative intensities.

Silica gel for column chromatography (-100, +200 mesh) was washed with hot water till sulphate-free, dried, activated at 125-30° for 6-8 hrs, and standardised.[49] Tlc was carried out on SiO_2-gel layers (0.25 mm) containing 15% gypsum and

and activated at 110-115° (2 hrs).

All the Wittig and Grignard reactions were carried out in an atmosphere of dry N_2.

2-Indanone; 12

To a soln of HCOOH (700 ml, 85%), and H_2O_2 (140 ml, 30%) was added with vigorous stirring, and maintaining the temp between 35-40°, indene 11 (117.3 ml) over a period of 2 hrs. After vigorous stirring for 7 hrs at room temp, HCOOH evaporated (b.p. 35-40°/20-25 mm), residue diluted with dil. H_2SO_4 (2 l, 7% by vol), and steam distilled. The white crystalline product from the distillate was collected on a sintered funnel, and dried (90 gms, 69%); m.p. 57-58° (lit.[14] m.p. 57-58°).

2-Indanol;13

(i) To a slurry of LAH (5.86 g) in dry ether (100 ml), was added with stirring, and cooling at 0°, a soln of the ketone 12 (20 g) in dry ether (250 ml), and further stirred for 1.5 hrs. This was then decomposed with Na_2SO_4 aq soln, and filtered. The residue was washed with ether (50 ml x 2), and filtered. The combined filterate was dried, and evaporated:

yellowish crystalline solid of 13 (18.9 g, 90%), m.p. 67-68° (lit.[12] 68-70°).

(ii) To a stirred soln of the ketone 12 (13.2 g) in CH_3OH (150 ml) at 25°, was added $NaBH_4$ (1.9 g) in portions (15 min), and stirred for 3 hrs, CH_3OH evaporated, residue diluted with H_2O (150 ml), extracted with $CHCl_3$ (75 ml x 3), washed, dried, and evaporated: yellowish crystalline solid of 13 (12.9 g, 90%), m.p. 67-68° (lit.[12] 68-70°). IR(CCl_4): OH 3460 cm^{-1}, 3080, 3035, 2970, 2920, 2850, 1490, 1468, 1430, 1340, 1310, 1260, 1165, 1045, 955, 932 cm^{-1}. PMR: CH_2, 4H, two q, 2.72 ppm, J_1=16Hz, J_2=4Hz; 3.05 ppm, J_1=17Hz, J_2=6Hz; CHOH, 1H, bm, 4.45 ppm, W_H=16Hz; OH, 1H, bs, 3.04 ppm.

2-Indanol acetate; 14

A mixture of the alcohol 13 (20g), Ac_2O (150 ml), and dry pyridine (10 ml) was warmed, and left overnight at room temp. Then decomposed with H_2O (300 ml), extracted with light petroleum (75 ml x 3), washed with H_2O (50 ml x 1), dil. HCl (50 ml x 1, 1:1), H_2O (50 ml x 3), washed, dried and evaporated: colorless liquid of 14 (31g, 95%). b.p. 120°(bath)/2 mm. R_f 0.65 (Tlc: 10% EtOAc in C_6H_6). IR (CCl_4): 3084, 3040, 2968, 2918, 2860, 2850 cm^{-1}, C=O 1748 cm^{-1}, 1492, 1470, 1430, 1382, 1254, 1220, 1195, 1055, 1035, 985 cm^{-1}.

PMR: $OCOCH_3$, 3H, ss, 1.94ppm; CH_2, 4H, two q, 2.93ppm, J_1= 16Hz, J_2=4Hz; 3.30 ppm, J_1=16Hz, J_2=6Hz; $CHOCOCH_3$, 1H, m, 5.46ppm, W_H=15Hz; Aromatic, 4H, s, 7.18 ppm.

5-Acetyl-2-indanol acetate; 15

To a cooled (0^o) soln of the acetate 14 (26.4 g), dry CS_2 (40 ml), and CH_3COCl (19.6 g) was added powdered anhydrous $AlCl_3$ (45.3 g) during 45 min and stirred for 3 hrs (the $AlCl_3$ was contained in a wide mouth flask attached to the reaction vessel by a short length wide bore Tygon tubing. In this way the solid could be added in controlled portions without exposure to the air). After stirring at room temp for 3 hrs, the reaction mixture was decomposed with cold H_2O, extracted with ether (150 ml x 3), washed, dried, and evaporated: white crystalline solid of 15 (30 g, 95%), b.p. 200-210°(bath)/1 mm. m.p. 64°. R_f 0.45 (Tlc: 10% EtOAc in C_6H_6). IR (CCl_4): 2970, 2918, 2860, 2840 cm^{-1}, C=O 1745, 1694 cm^{-1}, 1620, 1580, 1434, 1380, 1365, 1318, 1248, 1218, 1192, 1170, 1052, 1032, 980 cm^{-1}. PMR: $OCOCH_3$, 3H, ss, 1.95 ppm; $Ar.COCH_3$, 3H, ss, 2.47 ppm; CH_2, 4H, two q, 2.95 ppm, J_1=16Hz, J_2=4Hz; 3.27 ppm, J_1=17Hz, J_2=6Hz; $CHOCOCH_3$, 1H, bm, 5.46 ppm, W_H=15Hz; Aromatic, 3H, two d, 7.24 ppm, J=8Hz; 7.72 ppm, J=7Hz.

2,5-Diacetoxyindane; 16

To a stirred soln of HCOOH (60 ml, 85%), and H_2O_2 (14 ml,

30%), was added the ketone 15 (10.9 g) during 15 min, and stirred at room temp (22 hrs). HCOOH evaporated (b.p. 35-40°/ 20-25 mm): brownish liquid of formate-acetate and diol with R_f 0.70, 0.75, and 0.5 (Tlc: 50% EtOAc in C_6H_6), which was mixed with KOH (7 g), H_2O (5 ml), CH_3OH (50 ml), and refluxed for 5 hrs. CH_3OH evaporated, residue diluted with H_2O (100 ml), acidified with dil. HCl (1:1), extracted with EtOAc (75 ml x 3), washed, dried, and evaporated: brownish liquid of diol with R_f 0.5 (Tlc: 50% EtOAc in C_6H_6), which was acetylated with Ac_2O (30 ml), dry pyridine (5 ml), and left overnight at room temp. This was then decomposed with cold H_2O (150 ml), extracted with EtOAc (50 ml x 4), washed, dried, and evaporated: white crystalline solid of 16 (8.9 g, 75.5%), b.p. 180°(bath)/1mm, m.p. 70-71° (lit.[13] 72-73°). IR (CCl_4): 3035, 2970, 2918, 2868, 2842 cm^{-1}; C=O 1770, 1742 cm^{-1}; 1490, 1440, 1430, 1378, 1255, 1216, 1138, 1052, 1032, 980, 955, 900 cm^{-1}. PMR: $OCOCH_3$, 3H, ss, 1.95 ppm; $Ar.OCOCH_3$, 3H, ss, 2.18 ppm; $CHOCOCH_3$, 1H, m, 5.46 ppm, W_H=15Hz; CH_2, 4H, m, 2.76-3.5 ppm; Aromatic, 3H, two d, 6.82 ppm, J=9Hz; 7.12 ppm, J=7Hz. Mass: m/e 174 (M^+ - 60, 28.7%), 135 (38.8%), 134 (100%), 133 (35.7%), 119 (32.6%), 118 (99.2%), 117 (67.4%), 107 (35.7%), 105 (46.5%), 93 (31.8%), 79 (51.2%).

Indane-2,5-diol; 8

The diacetate 16 (10 g) was mixed with CH_3OH (60 ml),

KOH (6 g), H_2O (15 ml), and refluxed for 5 hrs. CH_3OH evaporated, residue diluted with H_2O (100 ml), acidified with dil. HCl (1:1), extracted with EtOAc (50 ml x 4), washed dried, and evaporated: crystalline solid of 8 (4.2 g, 65.6%), b.p. 215-220° (bath)/1mm, m.p. 112-113°. R_f 0.5 (Tlc: 50% EtOAc in C_6H_6). IR (KBr-pellet): (fig. 1): OH 3380 cm^{-1}; 3140, 2928, 2830, 1605, 1474, 1428, 1330, 1280, 1250, 1235, 1132, 1045, 940, 852, 810, 750 cm^{-1}. Mass: m/e 150 (M^+, 68.2%), 121 (27.1%), 108 (27.9%), 107 (61.2%), 94 (25.6%), 93 (100%), 92 (41.9%), 91 (43.4%), 80 (54.3%), 78 (38.8%), 54 (27.1%).

cis-Bicyclo(4,3,0)nonan-3,8-diol; 9

A mixture of aromatic diol 8 (13.9 g), EtOH (300 ml), 10% NaOH aq soln (10 ml), and Raney Ni, W_2 (2 g) was hydrogenated in Parr-apparatus at about 1600 psi at 155-160° for 8 hrs. After filtering out the catalyst, EtOH evaporated, residue diluted with H_2O (50 ml), neutralized with dil. HCl (1:1), extracted with EtOAc (75 ml x 3), washed dried, and evaporated: colorless thick liquid of 9 and hydrogenyled product (14 g) with R_f 0.2, and 0.8 (Tlc: 50% EtOAc in C_6H_6), which was placed on a silica gel column (30 cm x 4.5 cm), and eluted with EtOAc: C_6H_6 (1:1), EtOAc to yield hydrogenyled product (4 g), and the required saturated diol 9 (9.8 g, 68%). IR (Nujol): (Fig.2):

OH 3320 cm^{-1}, 2920, 2850, 1445, 1360, 1338, 1065, 1020, 970 cm^{-1}.

cis-Bicyclo(4,3,0)nonan-3,8-dione; 10

To a stirred soln of saturated diol 9 (7.7 g) in acetone (40 ml), was added Jone's reagent (17 ml), slowly at 5-8°, till the color of Jone's reagent persisted (6 hrs). This was then diluted with H_2O (15 ml), acetone evaporated, residue diluted with H_2O (75 ml), neutralized (solid $NaHCO_3$), extracted with $CHCl_3$ (75 ml x 3), washed, dried, and evaporated: colorless liquid of 10 (7.3 g, 96%), b.p. 150-155°(bath)/0.1 mm, n_D^{26} 1.4981, R_f 0.55 (Tlc: 50% EtOAc in C_6H_6). (96% purity by glc, 5% carbowax 20M, 6', 190°, 60 ml/min, R_t 5.0 min). IR (Fig. 3): (CCl_4): 3030, 2950 cm^{-1}, five-membered C=O 1755 cm^{-1}, six-membered C=O 1725 cm^{-1}, 1420, 1372, 1315, 1290, 1240, 1215, 1170, 1150 cm^{-1}. PMR (Fig. 4): CH,CH_2, 12H, bm, 1.6-3.0 ppm. Mass (Fig. 4A): m/e 152 (M^+, 100%), 123 (22.1%), 111 (32.9%), 96 (30%), 83 (21.4%), 70 (29.3%), 69 (95.7%), 68 (26.4%), 56 (83.6%), 55 (31.4%), 54 (21.4%). (Found: C, 72.5; H, 7.4. $C_9H_{12}O_2$ requires: C, 71.05; 7.89%).

3-Methylene-cis-bicyclo(4,3,0)nonan-8-one; 17

Methyl triphenyl phosphonium iodide: To a cold soln of Ph_3P (13.6 g) in dry C_6H_6 (80 ml) was added CH_3I (9.2 g), and left overnight at 10-15°. The separated ppt was filtered,

washed with C_6H_6, and dried: white crystalline solid (20.6g, 100%), m.p. 186-188°.

To a stirred suspension of freshly prepared K-t-butoxide (2.7 g) in dry C_6H_6 (130 ml) was added $Ph_3P^+MeI^-$ (8.88 g) and stirred at room temp, under N_2 for 30 min. The resulting intense yellow soln was transferred with dry N_2 into the addition funnel fitted with another flask which previously contained a stirred soln of the diketone 10 (3.0 g). The yellow phsphorane was then added slowly at 0-3° (1 hr), and further stirred for 2 hrs. After stirring at room temp (5 hrs), the brownish reaction mixture was decomposed with H_2O (50 ml), C_6H_6 layer separated, aq. layer extracted with light petroleum (75 ml x 3), washed, dried, and evaporated: semi-solid mass with Ph_3PO which was taken up in light petroleum (50 ml), digested on water bath (10 min), chilled at -10 to -15° (2 hrs), filtered, and evaporated: yellowish oil, which was placed on a silica gel column (20 cm x 2 cm), and eluted with light petroleum: C_6H_6 (1:1) to furnish colorless liquid of 17 (2.4 g, 80%), b.p. 90-92°(bath)/0.1 mm, n_D^{26} 1.5066, R_f 0.35 (Tlc: 30% light petroleum in C_6H_6). (95% purity by glc, 5% carbowax 20M, 6', 180°, 60 ml/min, R_t 2.5 min). IR (Fig. 5): (CCl_4): 2920 cm^{-1}, 5-membered C=O 1745 cm^{-1}, C=C 1658, 1450 cm^{-1}, 1410, 1150, 900 cm^{-1}. PMR (Fig. 6): $C\underline{H}_2$=C, 2H, d, 4.73 ppm,

J=6Hz; CH, CH_2, 12H, m, 1.6-2.5 ppm. Mass: m/e 150 (M^+, 100%), 108 (41.9%), 107 (54%), 95 (100%), 94 (43.5%), 93 (99.2%), 92 (56.5%), 91 (46%), 81 (54.8%), 80 (90.7%), 68 (44%). (Found: C, 79.5; H, 9.3. $C_{10}H_{14}O$ requires: C, 80; H, 9.33%).

3-Methyl-cis-bicyclo(4,3,0)non-2-ene-8-one; 18

A mixture of an olefin 17 (3 g), p-toluene-sulfonic acid (0.3 g), and dry C_6H_6 (50 ml) was refluxed for 10 hrs. The reddish reaction mixt was then diluted with H_2O (40 ml), neutralized ($NaHCO_3$), extracted with C_6H_6 (50 ml x 3), washed, dried, and evaporated: colorless liquid of 18 (2.6 g, 86.6%), b.p. 90-92°(bath)/0.1 mm, n_D^{26} 1.4988, R_f 0.35 (Tlc: 30% light petroleum in C_6H_6). (97% purity by glc, 5% carbowax 20M, 6', 180°, 60 ml/min, R_t 2.25 min). IR (Fig. 7): (CCl_4): 3010, 2922 cm^{-1}, 5-membered C=O 1745 cm^{-1}, C=C 1458, 1442 cm^{-1}, 1410 1385, 1220, 1115 cm^{-1}. PMR (Fig. 8): CH_3 C=C, 3H, bs, 1.68 ppm; CH=C, 1H, d, 5.36 ppm, J=2Hz; CH, CH_2, 10H, m, 1.51-2.4 ppm. Mass: m/e 150 (M^+, 40%), 122 (14%), 107 (40.7%), 94(100%), 93 (27.3%), 92 (33.3%), 82 (14.3%), 80 (40.7%), 78 (28%), 59 (33.3%), 54 (22.7%). (Found: C, 79.5; H, 7.3. $C_{10}H_{14}O$ requires: C, 80; H, 9.3%).

α-Acetyl-γ-butyrolactone[45]

(i) To a mechanically stirred soln of NaOH (20 g), H_2O (125 ml), EtOH (45 ml), was added a mixture of ethylene

oxide (22 g), and acetoacetic ester (65 g), (previously cooled to 0°) at $0-5^{\circ}$ (20 min), further stirred (2 hrs), and left at $0-5^{\circ}$ (48 hrs). The resulting soln was neutralized with HOAc (30 ml), extracted with C_6H_6 (75 ml x 3), washed, dried, evaporated, and fractionated: colorless liquid (18.2 g, 30%), b.p. $107-108^{\circ}$/5 mm (lit.[45] $107-108^{\circ}$/5 mm).

(ii) To a soln of Na (6 g) in EtOH (100 ml), was added a soln of acetoacetic ester (33 g) in EtOH (35 ml) slowly at room temp and refluxed for 30 min. To this soln was added a mixture of ethylene oxide (11 g), and EtOH (13 ml), (previously cooled to 0°), at $0-3^{\circ}$, further stirred (2 hrs), and left overnight. EtOH evaporated, residue neutralized with HOAc (1:1), extracted with C_6H_6 (50 ml x 4), washed, dried, evaporated, and fractionated: colorless liquid (16.2 g, 55%), b.p. $142-145^{\circ}$/30 mm (lit.[45] $142-145^{\circ}$/30 mm).

5-Chloro-2-pentanone[46]

A mixture of con. HCl (22.5 ml), H_2O (26.5 ml), and α-acetyl-γ-butyrolactone (19.2 g) was placed in a flask fitted with a bulb-type condenser, and a receiver immersed in an ice-water bath. CO_2 evolved, temp. of reaction mixture was raised at such a rate that it did not foam over into the condenser. After rapid collection of distillate (45 ml),

H_2O (25 ml) was added to the distilling flask, and another distillate (5 ml) was collected. The combined distillate was extracted with ether (50 ml x 4), dried ($CaCl_2$), and evaporated: colorless liquid (11.4 g, 89%), b.p. 70-75°/20 mm (lit.[46] 70-72°/20 mm).

(4,4-Ethylenedioxy)pentyl triphenyl phosphonium iodide; 19

A mixture of 5-cl-2-pentanone (11 g), acetone (80 ml), and NaI (42 g) was refluxed for 5 hrs and filtered. Acetone evaporated, residue diluted with ether (200 ml), washed with 10% $Na_2S_2O_3$ aq soln (25 ml x 1), washed, dried, and evaporated: brownish liquid of 5-I-2-pentanone (19.2 g).

To this iodide in dry C_6H_6 (100 ml), was added Ph_3P (26 g), and refluxed for 15 hrs. The precipitated 4-oxo-pentyl triphenyl phosphonium iodide was filtered, washed with little dry C_6H_6, and dried (33.4 g, 71.1%), m.p. 228-229°, (lit.[17b] m.p. 230°).

This ketophosphonium salt (33 g), p-toluenesulfonic acid (1 g), ethylene glycol (30 ml), and dry C_6H_6 (350 ml) were refluxed in a Dean-Stark unit for 24 hrs. This was then neutralized (solid K_2CO_3), C_6H_6 evaporated, and the residue shaken well with H_2O (300 ml) to precipitate fine white

crystals of the required phosphonium salt, 19 which was filtered and dried (30 g, 83.1%), m.p. 211-213° (lit.[17a] 211.5°).

6":8,6":12-cis-Cyclo-10-methyl-6-ethyl-3-5, cis-9-dodecadiene-2-one; 21

To a stirred suspension of freshly prepared K-t-butoxide (2.46 g) in THF (40 ml), was added the phosphonium salt 19 (10.36 g), and stirred at room temp (30 min), under N_2. A soln of ketone 18 (1.5 g) in THF (3 ml), was added to this orange-phosphorane soln, and stirred for 1 hr at room temp, and 3 hrs at 45-50°. After leaving for 12 hrs at room temp, THF from the reaction mixture was evaporated, residue diluted with H_2O (35 ml), extracted with light petroleum (40 ml x 4), washed, dried, and evaporated: semi-solid mass with Ph_3PO which was taken up in light petroleum (50 ml), digested (10 min), chilled at -10 to -15° (2 hrs), filtered, and evaporated: yellowish oil of 20 which stirred with acetone (20 ml), H_2O (5 ml), and p-toluene-sufonic acid (100 mg) for 12 hrs at room temp. Acetone evaporated, product diluted with H_2O (15 ml), neutralized (solid K_2CO_3), extracted with light petroleum (50 ml x 4), washed, dried, and evaporated: pale yellow oil which was filtered through a silica gel column (20 cm x 2 cm) with light petroleum: C_6H_6 (1:1) to yield colorless liquid of 21 (1.4 g, 70%), b.p. 150°(bath)/0.1 mm, n_D^{26} 1.5032. R_f 0.42 (Tlc: 30% light petroleum in C_6H_6).

(97% purity by glc, 5% carbowax 20M, 6', 200°, 60 ml/min, R_t 4.5 min). IR (Fig. 9): (CCl_4): 3008, 2920 cm^{-1}, C=O 1720 cm^{-1}, 1510 cm^{-1}, C=C 1440 cm^{-1}, 1412, 1370, 1235, 1170 cm^{-1}. PMR (Fig. 10): $C\underline{H}_3$ C=C, 3H, bs, 1.65 ppm; $C\underline{H}_3CO$, 3H, ss, 2.16 ppm; CH,CH_2, 14H, m, 1.4-2.6 ppm; $CH_3.C=C\underline{H}$, $C\underline{H}=C$, 2H, two bm, 5.12 ppm, W_H=17Hz; 5.30 ppm, W_H=13Hz. Mass: (Fig. 10A): m/e 218 (M^+, 87.5%), 162 (61.4%), 148 (55.7%), 145 (69.3%), 107 (71.6%), 106 (33%), 95 (100%), 94 (82.4%), 93 (63.1%), 80 (46%), 78 (40.9%), 72 (26.1%). (Found: C, 82.8; H, 10.3. $C_{15}H_{22}O$ requires: C, 82.57; H, 10.09%).

Methyl trans,trans,cis-and cis,trans,cis-7":9,7":13-cis-cyclo-7-ethyl-3,11-dimethyl-2,6,10-tridecatrienoate;22 and 23

Methyl diethyl phosphonoacetate was prepared from $(EtO)_3P$, and $BrCH_2COOMe$ by following the procedure described by Wolinsky, and Erickson[18] for triethyl phosphonoacetate.

To a stirred suspension of NaOMe (1.74g) in DMF (15 ml) was added $(EtO)_2P(O)CH_2COOMe$ (5.78 g) at 20-25°, and stirred for 1 hr, under N_2. A soln of ketone 21 (1.5 g) in DMF (3 ml) was added to this clear soln of the Na-salt of methyl diethyl phosphonoaceate, and stirred (24 hrs) at room temp. The resulting dark brown soln was diluted with H_2O (35 ml), extracted with light petroleum (25 ml x 5), washed, dried, and evaporated: pale yellow oil (1.6 g, 88.9%), which was chromatographed on

a silica gel column (13 cm x 2 cm) with light petroleum: C_6H_6 (1:1) to furnish a mixture of 22 and 23 (0.86 g). [100% purity by glc, 5% carbowax 20M, 6', 190°, 60 ml/min, R_f 5.5min (23, 25%), 6.75 min (22, 75%)], mixture of 22, 23 and 21 (0.265 g), and 21 (0.273 g).

Inverted-dry-column-chromatography separation of 22 and 23

A mixture of 22 and 23 (1 g) was applied to a column, and developed in the solvent system (light petroleum: C_6H_6, 60:40) upto the height of 20 cm at ~500 mm pressure. The digging of cuts (each 0.5 to 1 mm thickness) were made and thoroughly extracted with ether. Each cut was tested on tlc, and similar cuts were lined up. Results and detailed data are given below:

1.	Wt. of the mixture taken	... 1 g
2.	R_f (tlc) of components	... 0.62, 0.65
3.	Ratio of components, 22:23	... 75:25
4.	Wt. of silica gel taken	... 250 g
5.	Column dimension	... 24 cm x 4.6 cm
6.	Method of loading the mixture	... absorbed on silica gel (2 g)
7.	Solvent system, light petroleum:C_6H_6	... 40:60
8.	Time taken for development	... 2.5 hrs
9.	No. of cuts made for extraction	... 60
10.	Total recovery	... 95%

11. Wt of pure trans-(or E) component ... 470 mg

12. Wt of pure cis-(or Z) component ... 120 mg

13. Wt of pure mixture of 22 and 23 ... 260 mg

14. Wt of polymeric impurities ... 100 mg

15. Physical data: E-Ester 22: b.p. 170°(bath)/0.05 mm. n_D^{26} 1.5122. R_f 0.62 (Tlc: 40% light petroleum in C_6H_6). (94% purity by glc, 5% carbowax 20M, 6', 190°, 60 ml/min, R_t 6.75 min). IR (Fig. 11): (CCl_4): 2905 cm^{-1}, C=O 1720 cm^{-1}, C=C 1644, 1430 cm^{-1}, 1372, 1352, 1320, 1272, 1220, 1142, 1045, 915 cm^{-1}. PMR (Fig. 12): CH_3.C=C, 3H, bs, 1.64 ppm; Z-CH_3.C=C.COOMe, 3H, ss, 2.15 ppm; $COOCH_3$, 3H, ss, 3.61 ppm; CH, CH_2, 14H, m, 1.4-2.6 ppm; CH_3.C=CH, CH=C, 2H, m, 5.10 ppm, W_H=15Hz; 5.28 ppm, W_H=12 Hz; C=CH.COOMe, 1H, bs, 5.55 ppm, W_H=4Hz, Mass: m/e 274 (M^+, 44.3%), 161 (100%), 133 (50%), 119 (25%), 114 (74.2%), 105 (72.5%), 91 (58.2%), 81(54.9%), 79(49.6%), 77(37.7%), 55(28.7%), 41 (45.1%). (Found: C, 79.1; H, 9.1. $C_{18}H_{26}O_2$ requires: C, 78.83; H, 9.49%).

Z-Ester 23: b.p. 170°(bath)/0.05 mm. n_D^{26} 1.5097. R_f 0.65 (tlc: 40% light petroleum in C_6H_6). (92% purity by glc, 5% carbowax 20M, 6', 190°, 60 ml/min, R_t 5.5 min). IR (Fig. 13): (CCl_4): 2910 cm^{-1}, C=O 1718 cm^{-1}, C=C 1640, 1430 cm^{-1}, 1372, 1320, 1272, 1232, 1145, 1050, 915 cm^{-1}, C=C 850 cm^{-1}. PMR (Fig. 14): CH_3.C=C, 3H, bs, 1.64 ppm; E-CH_3.C=C.COOMe, 3H, ss, 1.88 ppm;

$COOCH_3$, 3H, ss, 3.62 opm; CH, CH_2, 14H, m, 1.5-2.8 ppm; $CH_3.C{=}CH$, $CH{=}C$, 2H, m, 5.16 ppm, W_H=11Hz; 5.27 ppm, W_H=13Hz. Mass: m/e 274 (M^+, 55.5%), 161 (100%), 159 (32.9%), 160 (32.3%), 133 (87.7%), 114 (60%), 105 (78.1%), 93 (71.6%), 91 (47.1%), 81 (47.1%), 79 (39.4%). (Found: C, 79.1; H, 9.1. $C_{18}H_{26}O_2$ requires: C, 78.83; H, 9.49%).

dl-Methyl 7":9, 7":13-cis-cyclo-cis-10,11-epoxy-7-ethyl-3,11-dimethyl-trans-2,6-6-tridecadienoate; 4

A soln of m-Cl-$PhCO_3H$ (131.6 mg, 65.5%) in CH_2Cl_2 (8 ml), was added to a soln of E-ester 22 (137 mg) in CH_2Cl_2 (5 ml) at 0°. The mixture was left to stand overnight at 0° in a refrigerator (preadjusted at 0°). This was then diluted with CH_2Cl_2 (15 ml), washed with 5% Na_2CO_3 aq soln, washed, dried, and evaporated: colorless oil (127 mg), which was purified by preparative layer chromatography (PLC: silica gel: 20 cm x 20 cm x 0.5 mm; solvent system: light petroleum: EtOAc, 18:2). Desired cis-perhydroindane analogue of JH-I 4 (41 mg) was obtained from a band at R_f 0.5. The starting trienoic-E-ester 22 (32 mg) was recovered from a band at R_f 0.73. The diepoxide 25 (9 mg) was obtained from a band at R_f 0.27. PMR examination of 4 indicated that it was contaminated with small amount of other isomeric epoxide 24 which was homogeneous

on TLC, and could not be separated. 4: IR (Fig. 15): (CCl_4): 2920 cm^{-1}, C=O 1720 cm^{-1}, C=C 1648, 1432 cm^{-1}, 1378, 1360, 1275, 1222, 1148, 1035, 920 cm^{-1}, C=C 860 cm^{-1}. PMR (Fig. 16): CH_3·C(—O)—C, 3H, ss, 1.26 ppm; Z-CH_3·C=C.COOMe, 3H, ss, 2.16 ppm; CH_3·C=C, 3H, bs, 1.66 ppm, is it due to contamination of 24?; $COOCH_3$, 3H, ss, 3.62 ppm; CH=C, 1H, m, 5.10 ppm, W_H=14Hz; 5.28 ppm, W_H = 10 Hz; C=CH·COOMe, 1H, bs, 5.58 ppm, W_H=8Hz; CH, CH_2, 15H, m, 1.4-2.9 ppm. Mass (Fig. 16A): m/e 290 (M^+, 11.5%), 159 (67.5%), 133 (100%), 114 (56.3%), 105 (55.6%), 93 (88.1%), 91 (64.7%), 81 (93.7%), 79 (75.8%), 57 (74.6%), 55(64.3%). (Found: C, 74.7; H, 9.2. $C_{18}H_{26}O_3$ requires; C, 74.48; H, 8.97%).

25: IR (CCl_4): 2918 cm^{-1}, C=O 1720 cm^{-1}, C=C 1644, 1430 cm^{-1}, 1374, 1355, 1220, 1145 cm^{-1}. PMR: CH_3·C(—O)—C, 3H, d, 1.25 ppm, J=3Hz; Z-CH_3·C=C.COOMe, 3H, ss, 2.15 ppm; $COOCH_3$, 3H, ss, 3.62 ppm; C=CH.COOMe, 1H, bs, 5.61 ppm; CH, CH_2, 16H, m, 1.45-2.87 ppm. Mass: m/e 306 (M^+, 2%), 183 (33.3%), 140 (38.1%), 109 (27.2%), 95 (32%), 93 (34%), 91 (24.5%), 81 (100%), 79 (36.7%), 55 (32%), 43 (70.7%).

cis-Bicyclo(4,3,0)nonan-3-ol-8-one; 26

To a well-stirred soln of the diketone 10 (6.0 g) in EtOH (100 ml) was added a soln of $NaBH_4$ (0.38 g) in EtOH (15 ml) at 0° during 20 min, and stirred for 2 hrs. H_2O (5 ml)

was added, EtOH evaporated, residue diluted with $CHCl_3$ (200 ml), washed, dried and evaporated: thick liquid (5.5 g) which was chromatographed on a silica gel column (60 cm x 2.5 cm), with C_6H_6 (50 ml x 2). C_6H_6: EtOAc-9:1 (50 ml x 2), 8:2 (50 ml x 2), 7:3 (50 ml x 4), 6:4 (50 ml x 6), 1:1 (50 ml x 10), 6:4 (50 ml x 10) to afford unreacted diketone 10 (0.405 g), required hydroxy ketone 26 (4.8 g, 77.9%), and diol 9 (0.376 g) at R_f 0.55, 0.35, and 0.2 respectively (Tlc: 50% EtOAc in C_6H_6). 26: b.p. 160-163°(bath)/0.1 mm, R_f 0.35 (Tlc: 50% EtOAc in C_6H_6). IR (Fig.17): ($CHCl_3$): OH 3460 cm^{-1}, 2990, 2940, 5-membered C=O 1740 cm^{-1}, 1625, 1460, 1412, 1375, 1170, 1060, 968 cm^{-1}. PMR ($CDCl_3$): C<u>H</u>OH, 1H, bm, 3.5-4.0 ppm; O<u>H</u> 1H, bs, 2.51 ppm; CH, CH_2, 12H, m, 1.2-2.6 ppm. Mass: m/e 154 (M^+, 79.6%), 136 (67.7%), 108 (96.8%), 95 (65.6%), 94 (100%), 93 (41.9%), 82 (40.9%), 79 (62.4%), 70 (36.6%), 67 (60.2%), 55 (36.6%), (Found: C, 70.8; H, 9.4. $C_9H_{12}O_2$ requires: C, 70.13; H, 9.09%).

<u>8-Methylene-cis-bicyclo(4,3,0)nonan-3-ol; 27</u>

To a stirred suspension of freshly prepared K-t-butoxide (7.1 g) in THF (70 ml) was added $Ph_3P^+CH_3I^-$ (24 g), and stirred under N_2 for 30 min. A soln of hydroxy ketone 26 (1.8 g) in THF (3 ml) was added to this intense yellow phosphorane soln, stirred (5 hr) at room temp and left overnight. THF evaoorated,

residue diluted with H_2O (25 ml), extracted with light petroleum (50 ml x 4), washed, dried and evaporated: semi-solid mass which was taken up in light petroleum (50 ml), digested at 50° (10 min), chilled at -10 to -15° (2 hrs), filtered, and evaporated: yellowish oil which was filtered through a silica gel colum (10 cm x 2) with light petroleum: C_6H_6 (1:1) to give colorless liquid of 27 (1.28 g, 70%), b.p. 110°(bath)/ 0.1 mm, n_D^{26} 1.5051. (94.8% purity by glc, 5% carbowax 20M, 6', 160°, 60 ml/min, R_t 3.68 min). IR (Fig. 18): (CCl_4):OH 3340 cm^{-1}, 3070, 2920, 2830 cm^{-1}, C=C 1660, 1452 cm^{-1}, 1432, 1368, 1320, 1292, 1240, 1162, 1060, 1010, 985 cm^{-1}, C=C 944 cm^{-1}, 926, 878 cm^{-1}. PMR (Fig. 19): CHOH, 1H, m, 3.3-4.0 ppm; OH, 1H, bs, 2.82 ppm; CH, CH_2, 1H, m, 1.06-2.64 ppm. Mass: m/e 152 (M^+, 23.9%), 138 (100%), 119 (47.9%), 106 (42.3%), 105 (26.1%), 94 (29.6%), 93 (98.6%), 92 (63.4%), 91 (46.5%), 79 (50.7%), 78 (57.7%). (Found: C, 79.9; H, 9.9. $C_{10}H_{16}O$ requires: C, 78.95; H, 10.53%).

8-Methylene-cis-bicyclo(4,3,0)nonan-3-one; 28

To a soln of olefinic alcohol 27 (1.5 g) in CH_2Cl_2 (60 ml), was added CrO_3-Py.complex supported on silica gel (28.6 g; 2.8g reagent contained 400 mg of CrO_3; 4 eq.), and shaken at room temp (20 hrs). The reagent was filtered off, and washed with CH_2Cl_2 (20 ml x 3). The combined washings

were washed with dil. HCl, 1:1 (25 ml x 1), H_2O (25 ml x 2), washed, dried and evaporated: colorless liquid of 28 (1.1 g, 75%), b.p. 90°(bath)/0.1 mm. n_D^{26} 1.4966. (98% purity by glc, 10% SE 30, 6', 170°, 60 ml/mm, R_t 6.08 min; 92% purity by glc, 5% carbowax 20M, 6', 60 ml/min, R_t 3.2 min). IR (Fig. 20): (CCl_4): 3060, 2930 cm^{-1}, 6-membered C=O 1720 cm^{-1}, C=C 1652 cm^{-1}, 1430, 1358, 1342, 1330, 1278, 1230, 1142, 882 cm^{-1}. PMR (Fig. 21): CH_2=C, 2H, d, 4.85 ppm, J=2Hz; CH, CH_2, 12H, m, 1.6-2.5 ppm. Mass: m/e 150 (M^+, 36.8%), 107 (11.8%), 95 (13.2%), 94 (11.8%), 93 (42.4%), 92 (100%), 91 (10.4%), 80 (25.7%), 79 (23.6%), 77 (7.6%), 55 (8.3%), (Found: C, 80.2; H, 9.9. $C_{10}H_{14}O$ requires: C, 80; H, 9.33%).

8-Methyl-cis-bicyclo(4,3,0)non-8-ene-3-one;29 and
8-Methyl-cis-bicyclo(4,3,0)non-7-ene-3-one; 30

This was prepared from 28 (3 g) in the same manner as described for 18 in 85% yield, b.p. 90°(bath)/0.1 mm. R_f 0.35 (Tlc: 30% light petroleum in C_6H_6). (96% purity by glc, 5% carbowax 20M, 6', 130°, 60 ml/min, R_t 6.56 min (29, 65%), 7.36 min (30, 35%).

GLC Separation of 29 and 30

The mixture (28 + 29) immediately described above was separated by preparative gas chromatography (Glc: 20% carbowax

20M on chromosorb W (45-60 mesh), 12' x 3/8", Al, 160°, 100 ml/min). The compound 29 showed following physical properties: b.p. 90-92°(bath)/0.1 mm. n_D^{26} 1.4919 (99% purity by glc, 10% carbowax 20M, 6', 170°, 60 ml/min, R_t 5.6 min). IR (Fig. 22): (CCl_4): 2918, six-membered C=O 1710 cm^{-1}, C=C 1438 cm^{-1}, 1400, 1372, 1330, 1315, 1220, 1120, 1005, 925 cm^{-1}, C=C 855 cm^{-1}. PMR (Fig. 23): Me.C=CH, 3H, d, 1.70 ppm, J=1Hz; CH,CH_2, 10H, m, 1.3-3.2 ppm; Me.C=CH, 1H, d, 5.13 ppm, J=2Hz. Mass (Fig. 23A): m/e 150 (M^+, 19%), 107 (19.7%), 95 (12.4%), 94 (21.2%), 93 (96.4%), 92(32.1%), 91 (35.8%), 80(100%), 79 (75.2%), 77 (43.1%), 57 (16.8%). (Found: C, 80.3; H, 10. $C_{10}H_{14}O$ requires: C, 80; H, 9.33%).

The compound 30 showed following physical properties: b.p. 90-92°/0.1 mm. n_D^{26} 1.4950. (97% purity by glc, 10% carbowax 20M, 6', 170°, 60 ml/min, R_t 6.24 min). IR (Fig.24): (CCl_4): 2916, six-membered C=O 1710 cm^{-1}, C=C 1440 cm^{-1}, 1400, 1372, 1312, 1224, 1010, 955, 875 cm^{-1}. PMR (Fig. 25): CH_3.C=CH, 3H, d, 1.70 ppm, J=1Hz; Me.C=CH, 1H, d, 5.12 ppm, J=2Hz; CH,CH_2, 10H, m, 1.8-3.2 ppm. Mass (Fig. 25A): m/e 150 (M^+, 66.7%), 135 (15.5%), 107 (56%), 95 (26.2%), 94 (25%), 93 (100%), 92 (31%), 91 (23.8%), 80 (13.1%), 79 (20.2%), 77 (14.3%), 65 (14.3%). (Found: C, 80.1; H, 9.8. $C_{10}H_{14}O$ requires: C, 80; H, 9.33%).

6":12,8:12-cis-Cyclo-10-methyl-6-ethyl-ξ-5, cis-9-dodecadiene-2-one; 32

This was prepared from 29 (0.75 g) in the same manner as described for 21 in 74% yield, b.p. 150-155°(bath)/0.1 mm. n_D^{26} 1.4990. R_f 0.42 (Tlc: 30% light petroleum in C_6H_6). (98% purity by glc, 5% carbowax 20M, 6', 190°, 60 ml/min, R_t 4.96 min). IR (Fig. 26): (CCl_4): 2940, 2870 cm^{-1}, C=O 1730 cm^{-1}, C=C 1450 cm^{-1}, 1365, 1252, 1166 cm^{-1}, C=C 868 cm^{-1}. PMR (Fig. 27): Me.C=C, 3H, bs, 1.70 opm; $COCH_3$, 3H, ss, 2.05 ppm; CH, CH_2, 14H, m, 1.2-2.9 ppm Me.C=CH, CH=C, 2H, bm, 5.10 ppm, W_H=2Hz. Mass (Fig. 27A): m/e 218 (M^+, 73.1%), 200 (19.4%), 160 (35.5%), 145 (25.8%), 133 (59.1%), 105 (17.2%), 94 (15.1%), 93 (96.8%), 92 (18.3%), 81 (20.4%), 80 (100%). (Found: C, 82.6; H, 10.2. $C_{15}H_{22}O$ requires: C, 82.57; H, 10.09%).

Methyl trans-ξ,cis- and cis,ξ,cis-7":13, 9:13-cis-cyclo-7-ethyl-3,11-dimethyl-2,6,10-tridecatrienoate; 33 and 34

Trimethyl phosphonoacetate (1.16 g) was added to a stirred suspension of NaOMe (0.347 g) in DMF (6 ml), under N_2, and stirred for 30 min at room temp (30°). To this clear soln of sodium enolate was added a soln of ketone 32 (0.7 g) in DMF (2 ml) at 20°, and stirred (24 hr) at room temp. This was then decomposed with H_2O (20 ml), extracted with ether (20 ml x 4), washed, dried, and evaporated: colorless liquid of 32 and

33 (0.624 g; 71%), b.p. 170°(bath)/0.05 mm. R_f 0.63, 0.66 (Tlc: 30% light petroleum in C_6H_6). (96% purity by glc, 5% carbowax 20M, 6', 190°, 60 ml/min, R_t 8.64 min)(34, 34%), 11.2 min (33,66%).

Inverted-dry-column-chromatography separation of 33 and 34

These isomers (600 mg) were separated in the same manner as described for the separation of 22 and 23. The E-ester 33 showed the following physical properties: b.p. 170°(bath)/ 0.05 mm. n_D^{26} 1.5084. R_f 0.63 (Tlc: 30% light petroleum in C_6H_6). (95% purity by glc, 5% carbowax 20M, 6', 190°, 60 ml/ min, R_t 11.2 min). IR (Fig. 28): (CCl_4): 2960, 2880, 2860 cm^{-1}, C=O 1735 cm^{-1}, C=C 1660, 1450 cm^{-1}, 1390, 1370, 1340, 1262, 1240, 1162, 968, 872 cm^{-1}. PMR (Fig. 29): Me.C=C, 3H, bs, 1.70 ppm; Z-Me.C=C.COOMe, 3H, ss, 2.13 ppm; COOMe, 3H, ss, 3.62 ppm; CH,CH_2, 14H, m, 1.2-3.0 ppm; Me.C=CH, CH=C, 2H, bm, 5.11 ppm, W_H=17Hz; C=CH.COOMe, 1H, bs, 5.57 ppm. Mass: m/e 274 (M^+, 97.8%), 161 (100%), 160 (22.2%), 145 (18.2%), 133 (50.5%), 119 (18.2%), 114 (39.4%), 105 (26.8%), 93 (63.6%), 81 (22.2%), 80 (40.4%). (Found: C, 78.5; H, 10.1. $C_{18}H_{26}O_2$ requires: C, 78.83; H, 9.49%).

The Z-ester 34 exhibited the following physical properties: b.p. 170°(bath)/0.05 mm. n_D^{26} 1.5080. R_f 0.66 (Tlc: 30% light

petroleum in C_6H_6) (94% purity by glc, 5% carbowax 20M, 6', 190°, 60ml/min, R_t 8.64 min). IR (Fig. 30): (CCl_4): 2930, 2860, 2840 cm^{-1}, C=O 1730 cm^{-1}, C=C 1652, 1450 cm^{-1}, 1440, 1380, 1365, 1325, 1240, 1230, 1196, 1165, 1090, 1065, 926 cm^{-1}, C=C 870 cm^{-1}. PMR (Fig. 31): Me.C=C, 3H, bs, 1.70 ppm; E-Me.C=C.COOMe, 3H, ss, 1.88 ppm, COOMe, 3H, ss, 3.62 ppm; CH,CH_2, 14H, m, 1.2-2.9 ppm; Me.C=CH, CH=C, 2H, bm, 5.11 ppm, W_H=13Hz; C=CH.COOMe, 1H, bs, 5.57 ppm. Mass: m/e 274 (M^+, 90.4%), 161 (100%), 160 (20.6%), 133 (65.4%), 132 (17.6%), 119 (24.3%), 144 (44.1%), 105 (40.4%), 93 (86.8%), 91 (19.9%), 81 (39.7%), 80 (80.1%). (Found: C, 78.8; H, 9.5. $C_{18}H_{26}O_2$ requires: C, 78.83; H, 9.49%).

dl-Methyl 7":13,9:13-cis-cyclo-cis-10,11-epoxy-7-ethyl-3,11-dimethyl-trans-2,6-6-tridecadienoate; 5

This was prepared from the E-ester 33 (137 mg) in the same manner as described for 4.

5 displayed following physical properties: R_f 0.5 (Tlc: light petroleum: EtOAc, 18:2). IR (Fig. 32): (CCl_4): 2940, 2864 cm^{-1}, C=O 1730 cm^{-1}, C=C 1656, 1442 cm^{-1}, 1381, 1362, 1330, 1252, 1230, 1155, 1085, 912 cm^{-1}, C=C, 868 cm^{-1}. PMR (Fig. 33): Me.C(—O—)C, 3H, ss, 1.35 ppm; Z-Me.C=C.COOMe, 3H, bs, 2.16 ppm; COOMe, 3H, ss, 3.62 ppm; Me.C=C, 3H, bs, 1.70 ppm,

is it due to contamination of 35?; Me.C(—O—)CH, CH, CH_2, 14H, m, 1.43-3.31 ppm; CH=C , 1H, m. 5.0 ppm, W_H=21Hz; C=CH.COOMe, 1H, d, 5.57 ppm, J=4Hz. Mass (Fig. 33A): m/e 290 (M^+, 15.2%), 177 (40.2%), 133 (42.9%), 119 (60.7%), 114 (46.4%), 105 (41.1%), 93 (100%), 92 (70.5%), 91 (70.5%), 81 (72.3%), 80 (53.6%), 79 (66.1%). (Found: C, 74.3; H, 8.94. $C_{18}H_{26}O_3$ requires: C, 74.48; H, 8.97%).

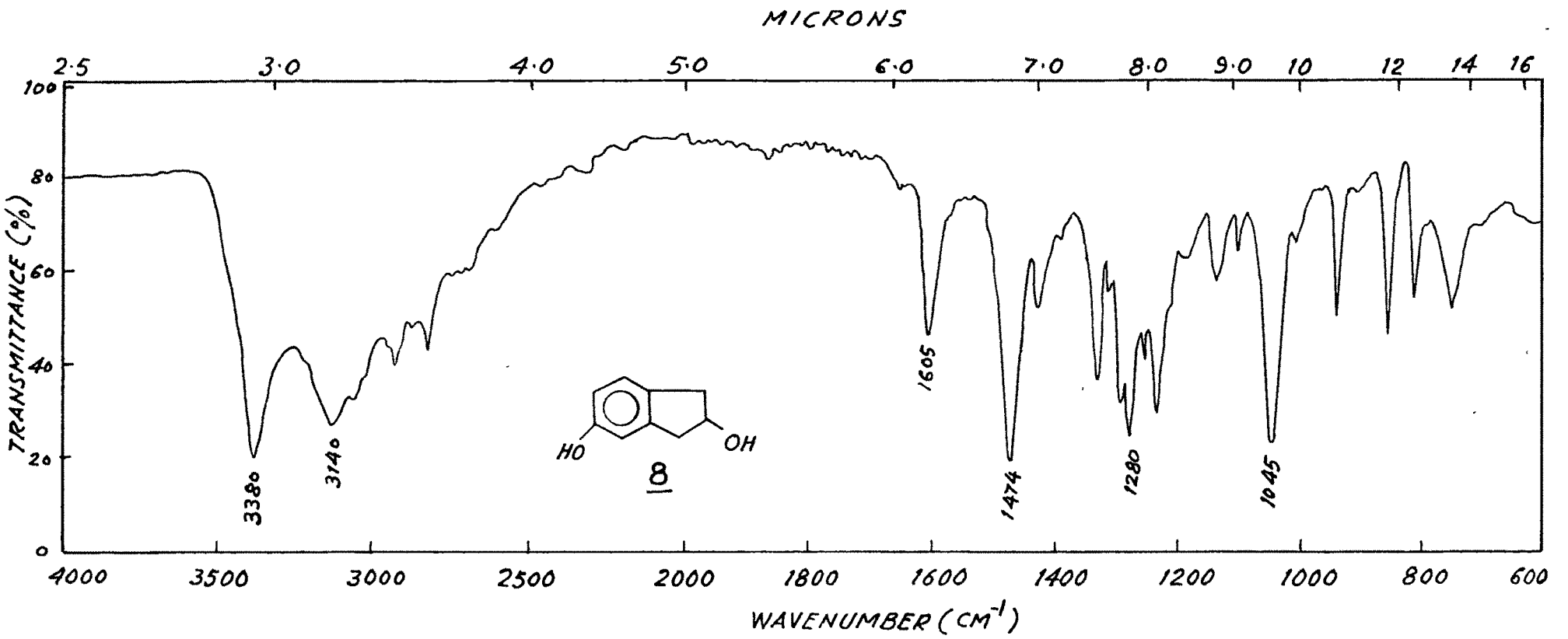


FIG. 1: IR SPECTRUM OF INDANE-2,5-DIOL 8

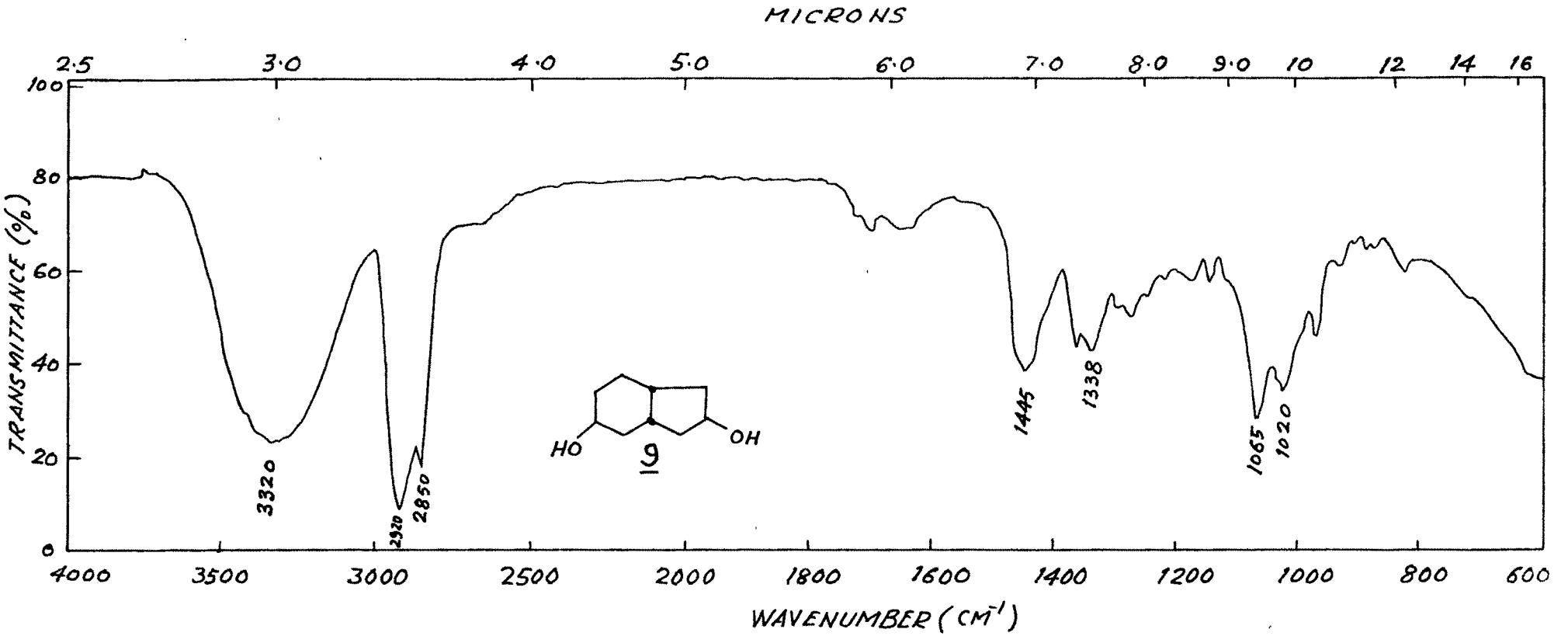


FIG. 2: IR SPECTRUM OF 3,8-DIHYDROXY BICYCLO(4,3,0) NONANE 9

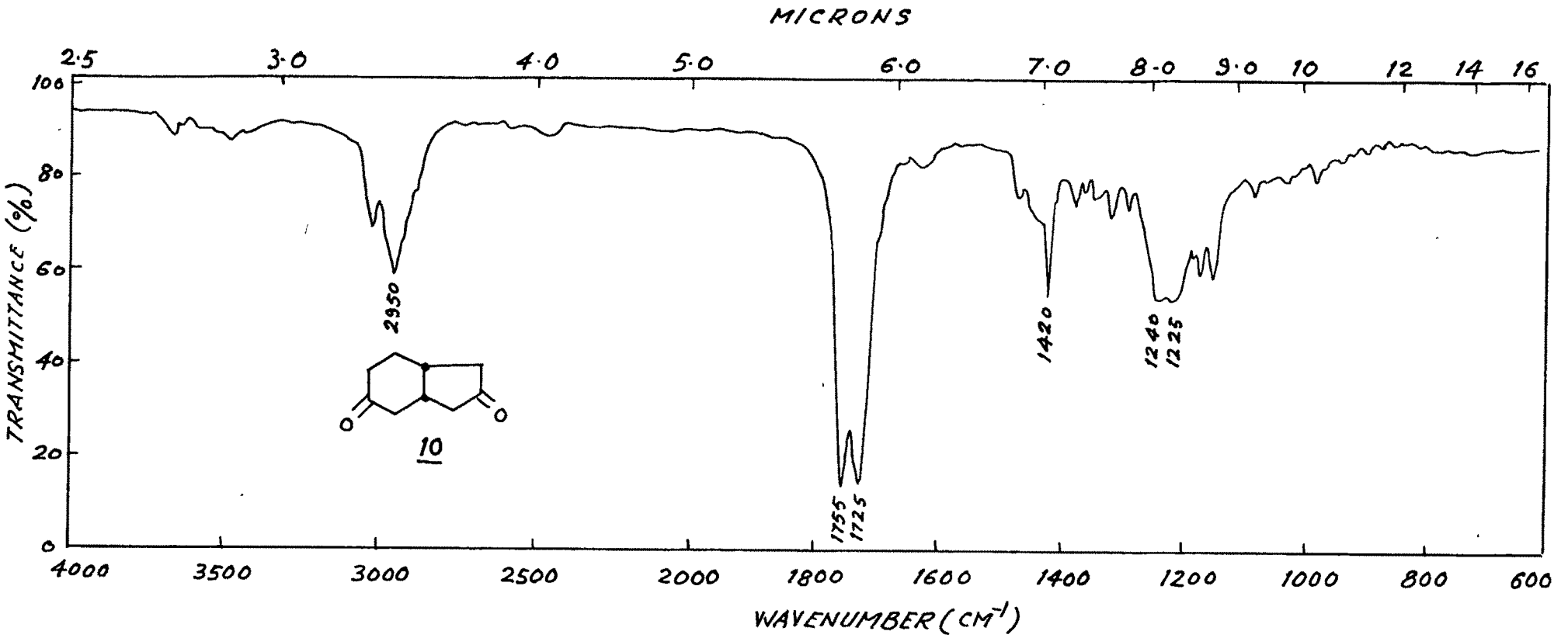


FIG. 3: IR SPECTRUM OF CIS-BICYCLO (4,3,0) NONAN-3,8-DIONE 10

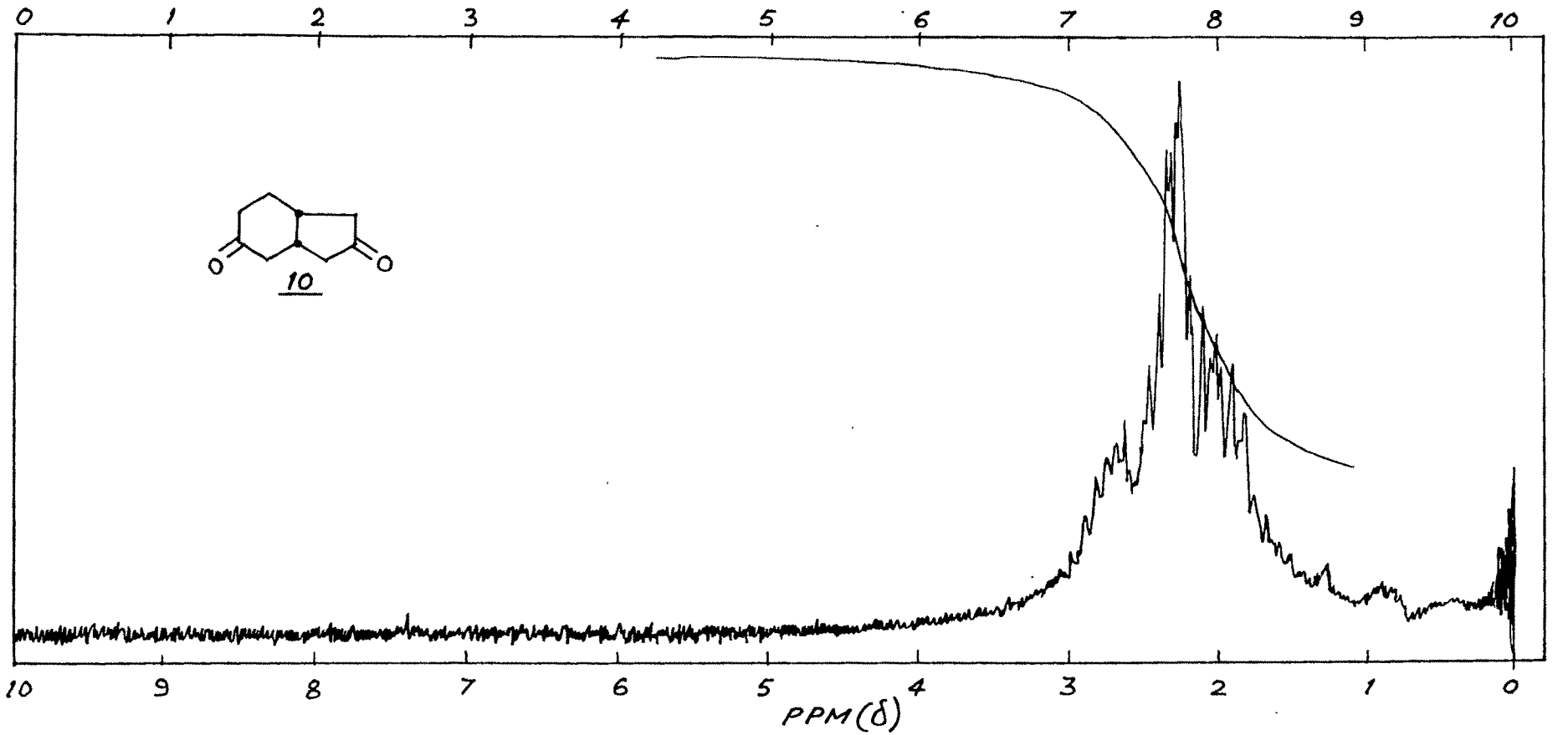


FIG.4 : NMR SPECTRUM OF CIS - BICYCLO(4,3,0) NONAN - 3,8 - DIONE 10

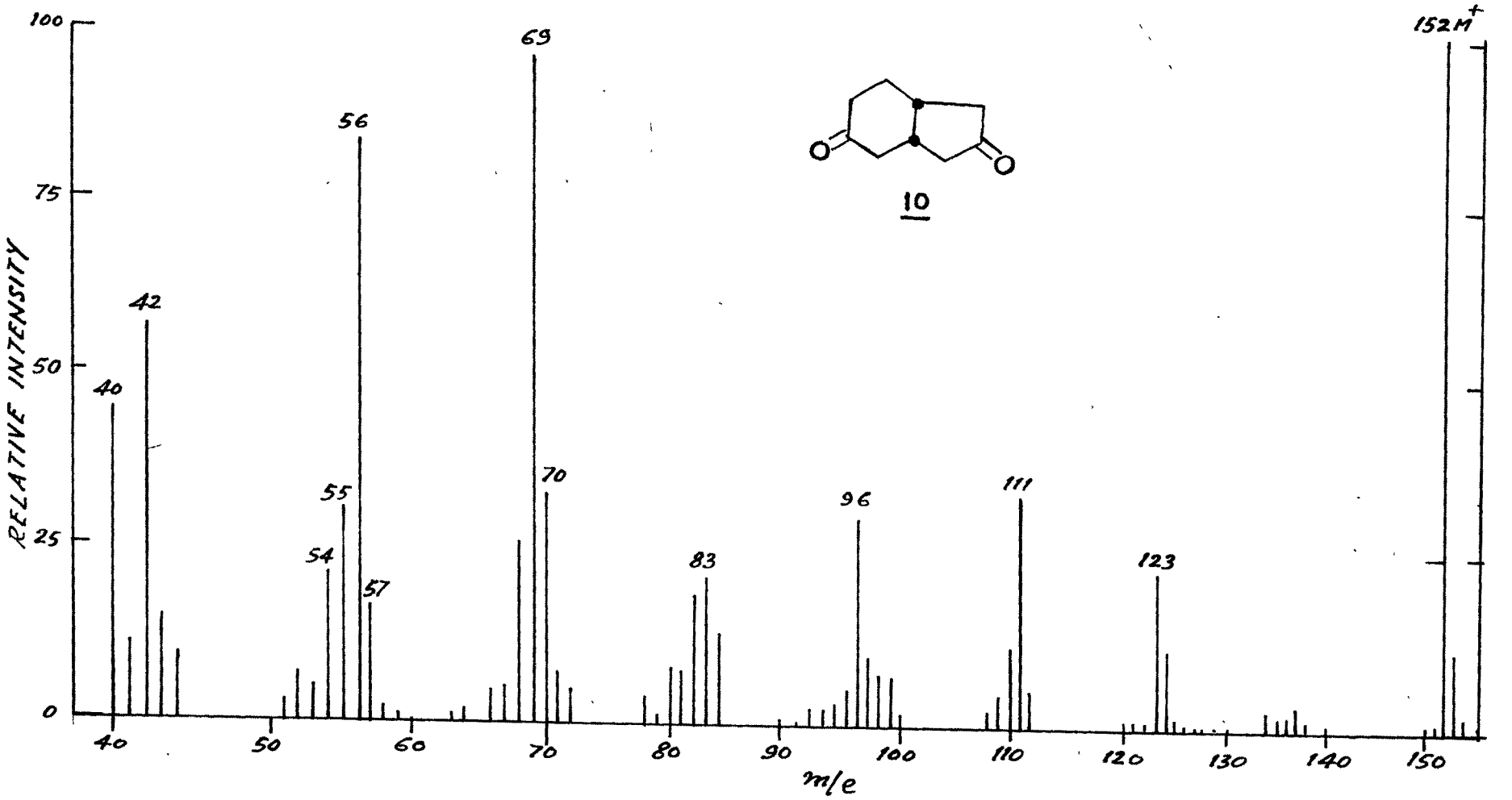


FIG. 4 A - MASS SPECTRUM OF CIS-BICYCLO (4,3,0) NONAN-3,8-DIONE; 10

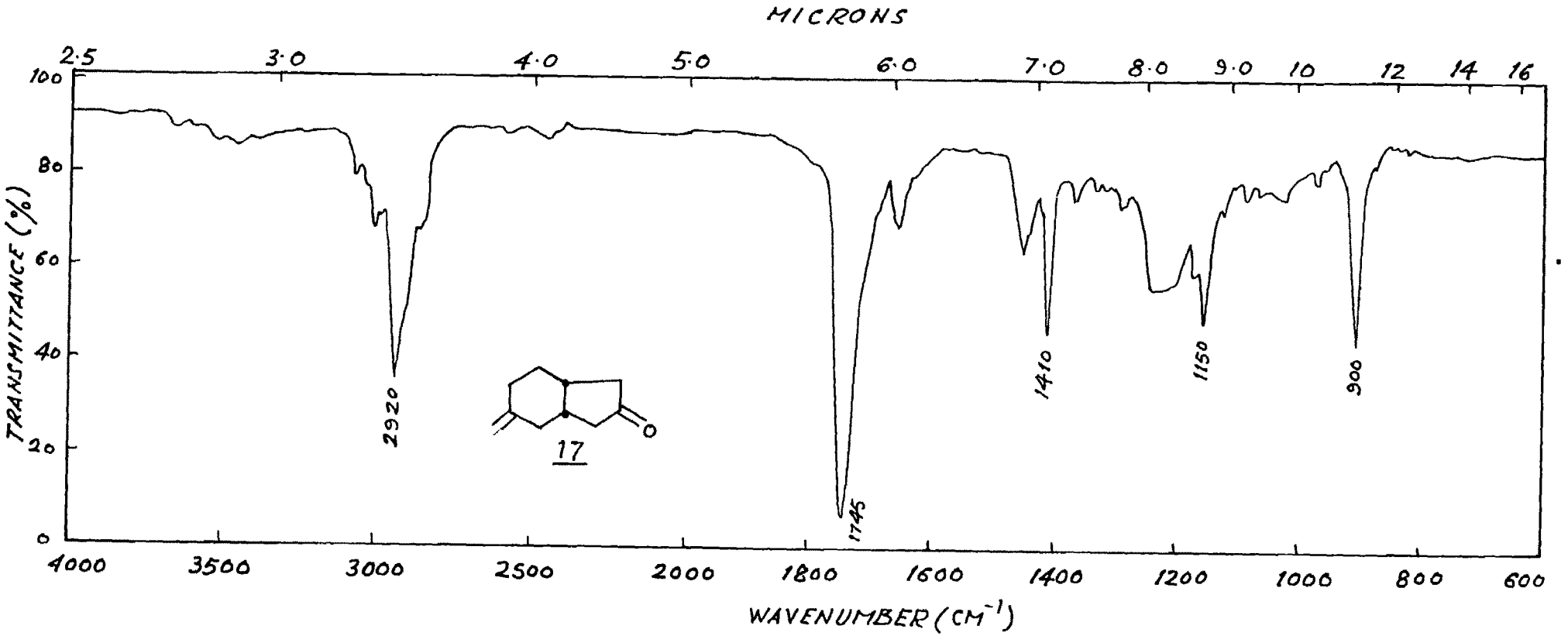


FIG. 5: IR SPECTRUM OF 3-METHYLENE-CIS-BICYCLO(4,3,0)NONAN-8-ONE 17

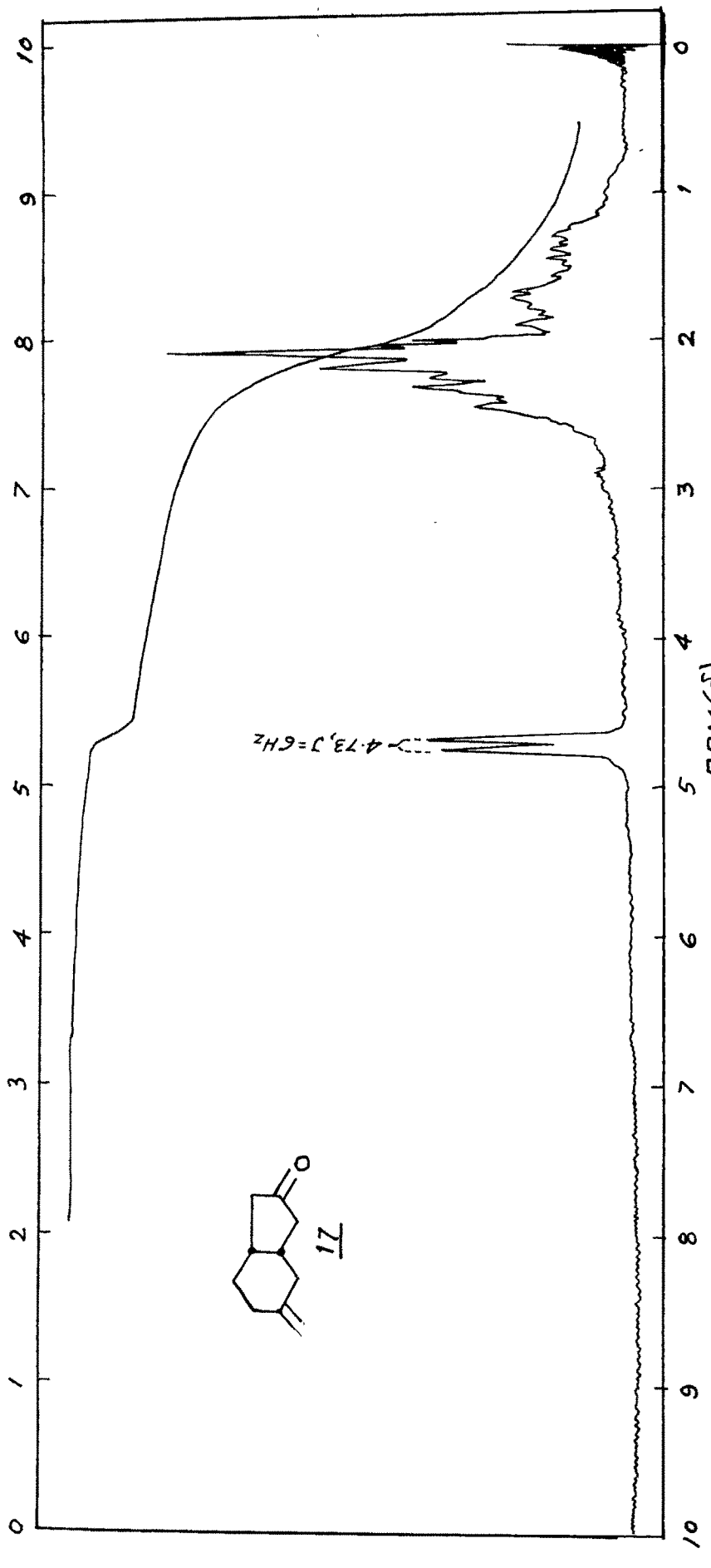


FIG.6: NMR SPECTRUM OF 3-METHYLENE-CIS-BICYCLO(4,3,0)NONAN-8-ONE 17

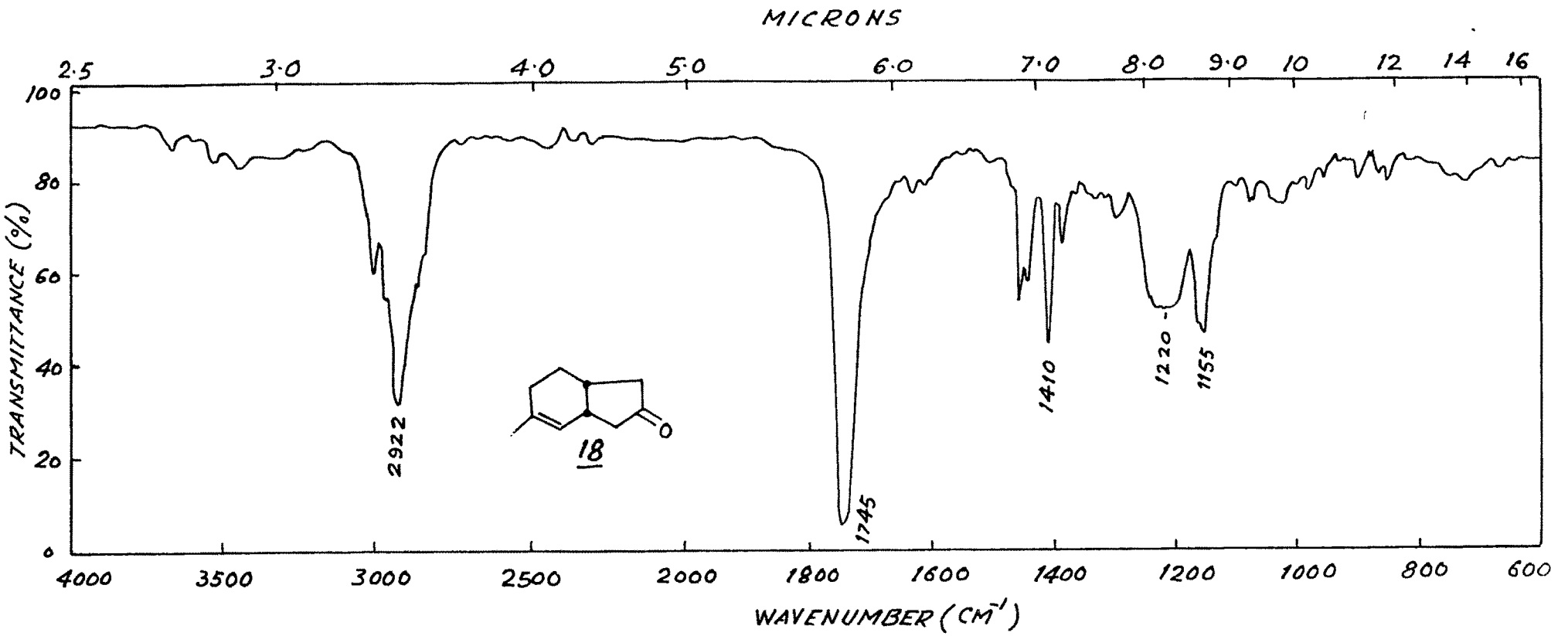


FIG. 7 : IR SPECTRUM OF 3-METHYL-CIS-BICYCLO(4,3,0)NON-2-ENE-8-ONE 18

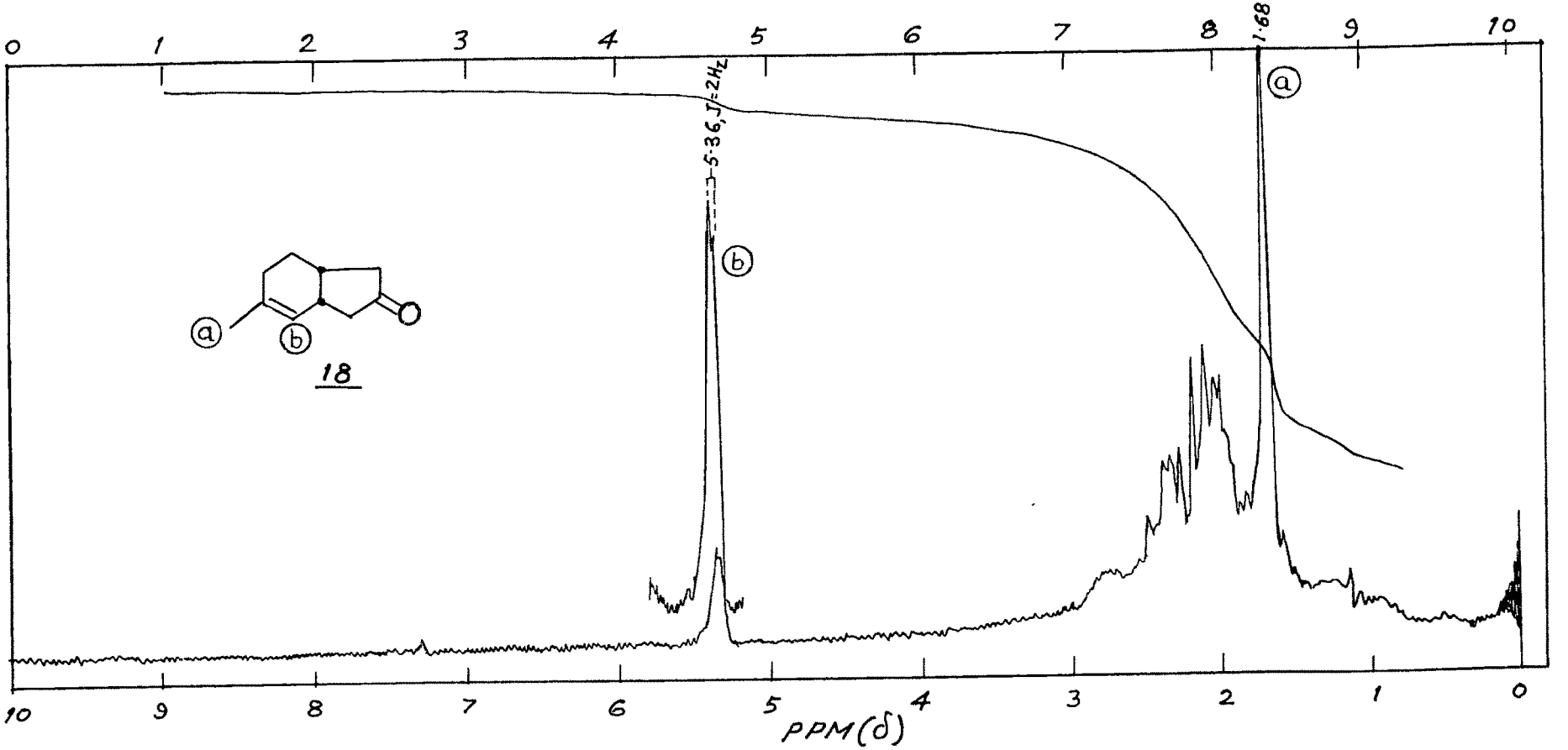


FIG.8: NMR SPECTRUM OF 3-METHYL - CIS - BICYCLO(4,3,0) NON-2-ENE-8-ONE 18

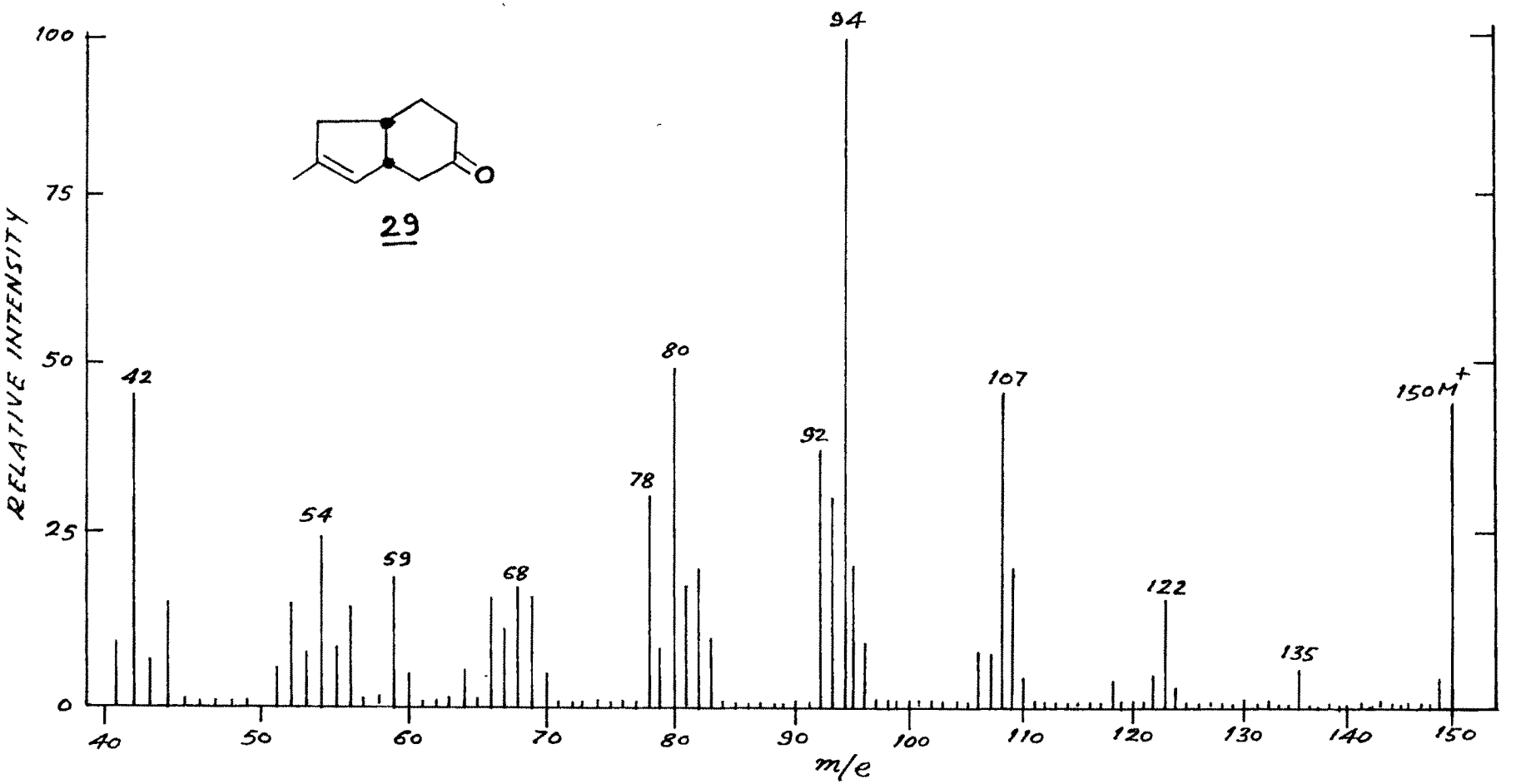


FIG. 8 A - MASS SPECTRUM OF 3-METHYL-CIS-BICYCLO(4,3,0)NON-3-EN-8-ONE, 29

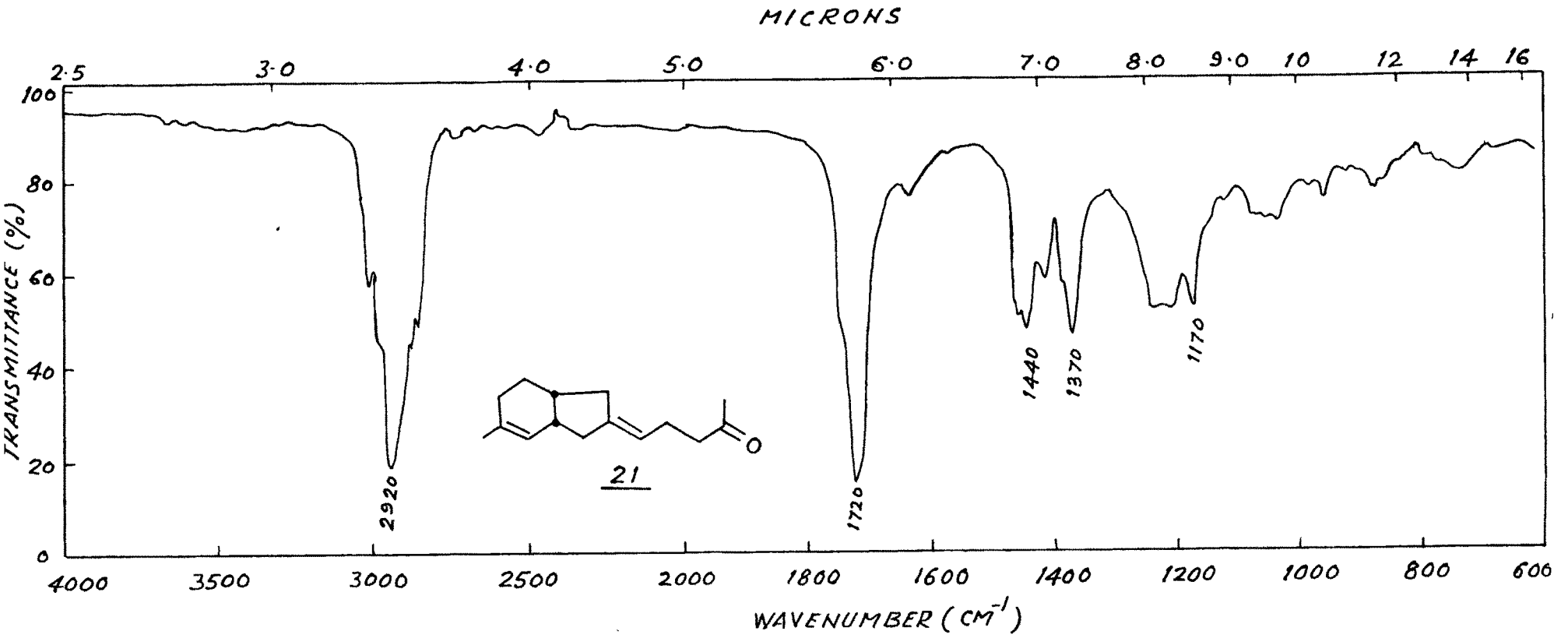


FIG. 9: IR SPECTRUM OF 6'':8, 6'':12 - CIS - CYCLO - 10 - METHYL - 6 - ETHYL - ξ - 5, CIS - 9 - DODECADIENE - 2 - ONE 21

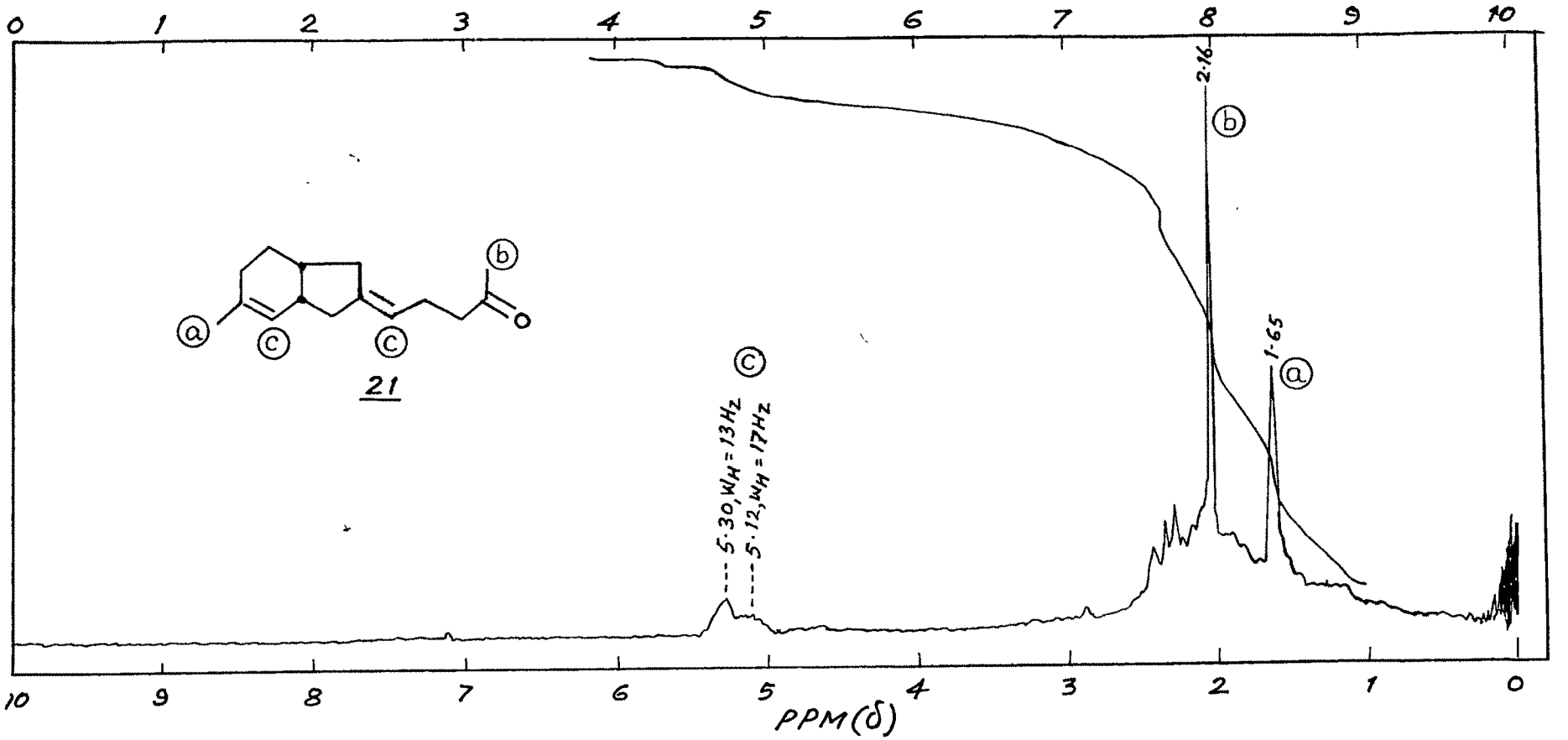
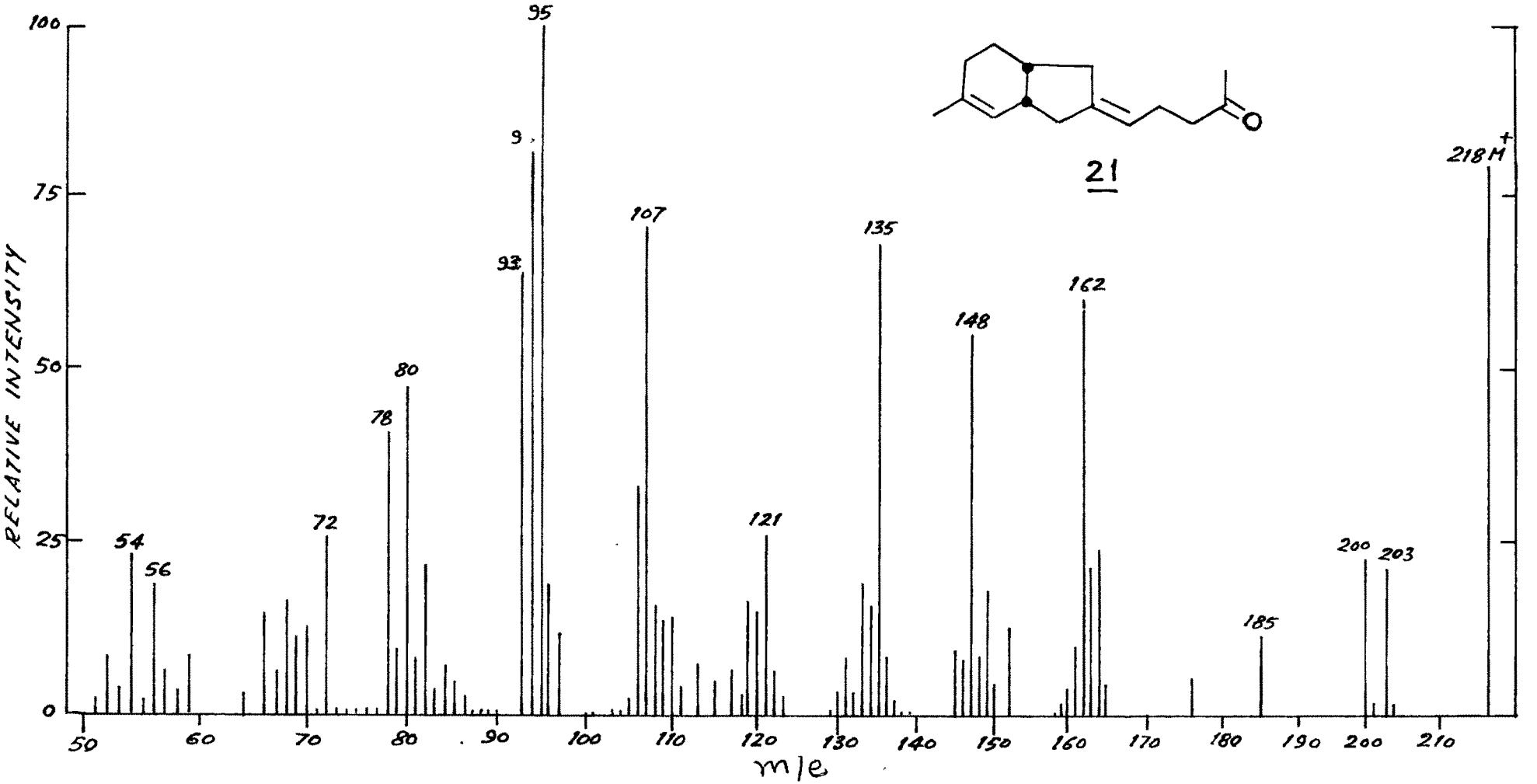


FIG. 10: NMR SPECTRUM OF 6'':8, 6'':12 - CIS - CYCLO - 10 - METHYL - 6 - ETHYL - § - 5, CIS - 9 - DODECADIENE - 2 - ONE 21



21

FIG. 10 A - MASS SPECTRUM OF 6":8,6":12-CIS-CYCLO-10-METHYL-6-ETHYL-E-5,CIS-9-DODECADIENE-2-ONE; 21

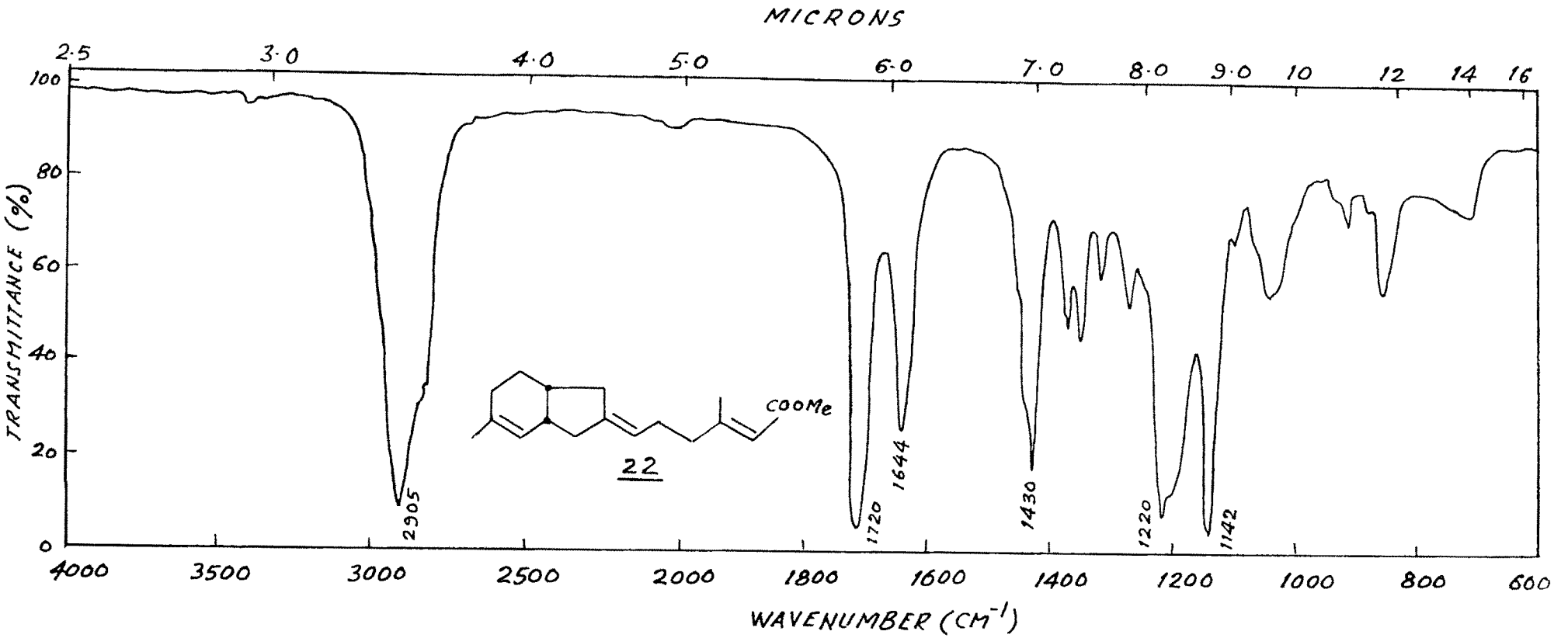


FIG. 11: IR SPECTRUM OF METHYL 7":9,7":13-CIS-CYCLO-7-ETHYL-3,11-DIMETHYL-TRANS-2,E-6,CIS-10-TRIDECATRIENOATE 22

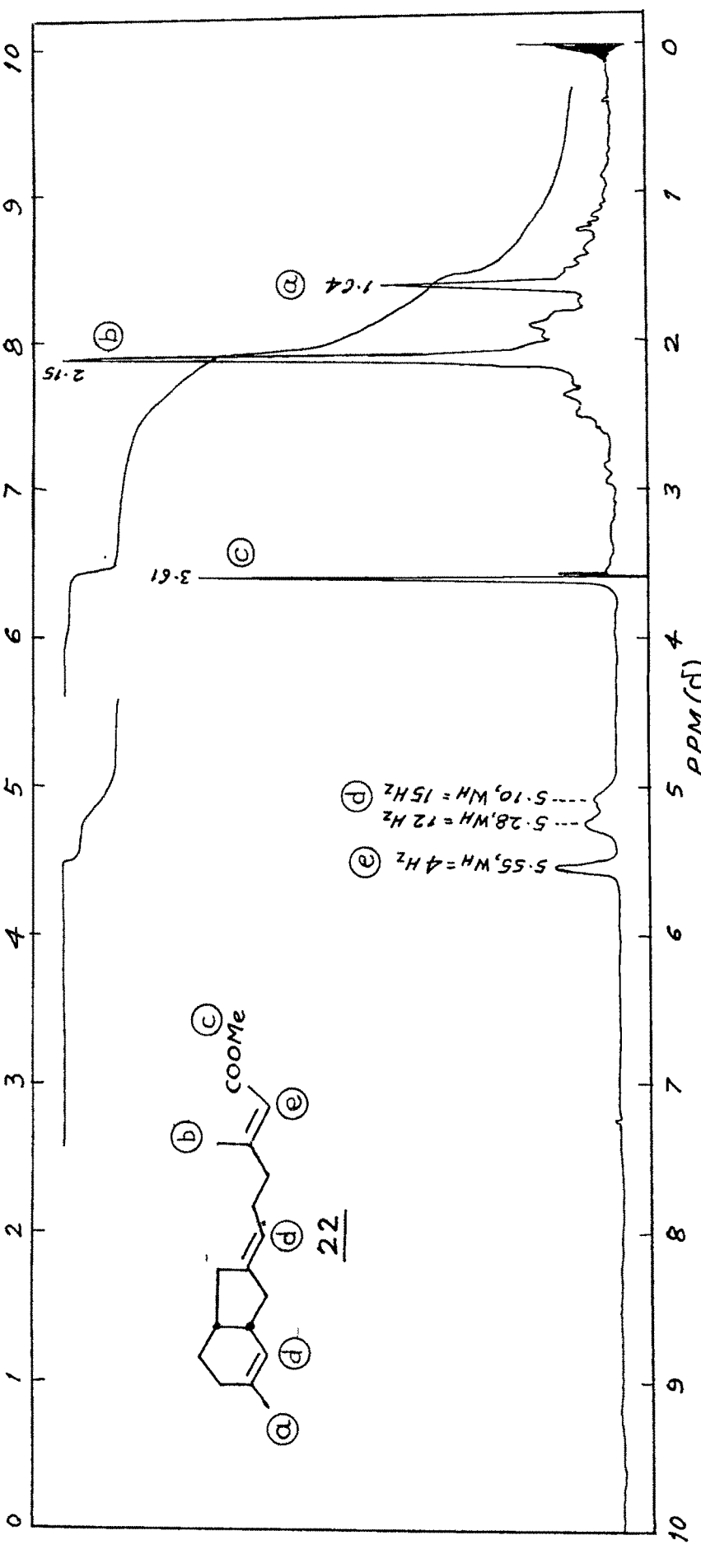


FIG. 12: NMR SPECTRUM OF METHYL 7:9, 7':13-CIS-CYCLO-7-ETHYL-3, 11-DIMETHYL-TRANS-2, E-6, CIS-10-TRIDECATRIENOATE 22

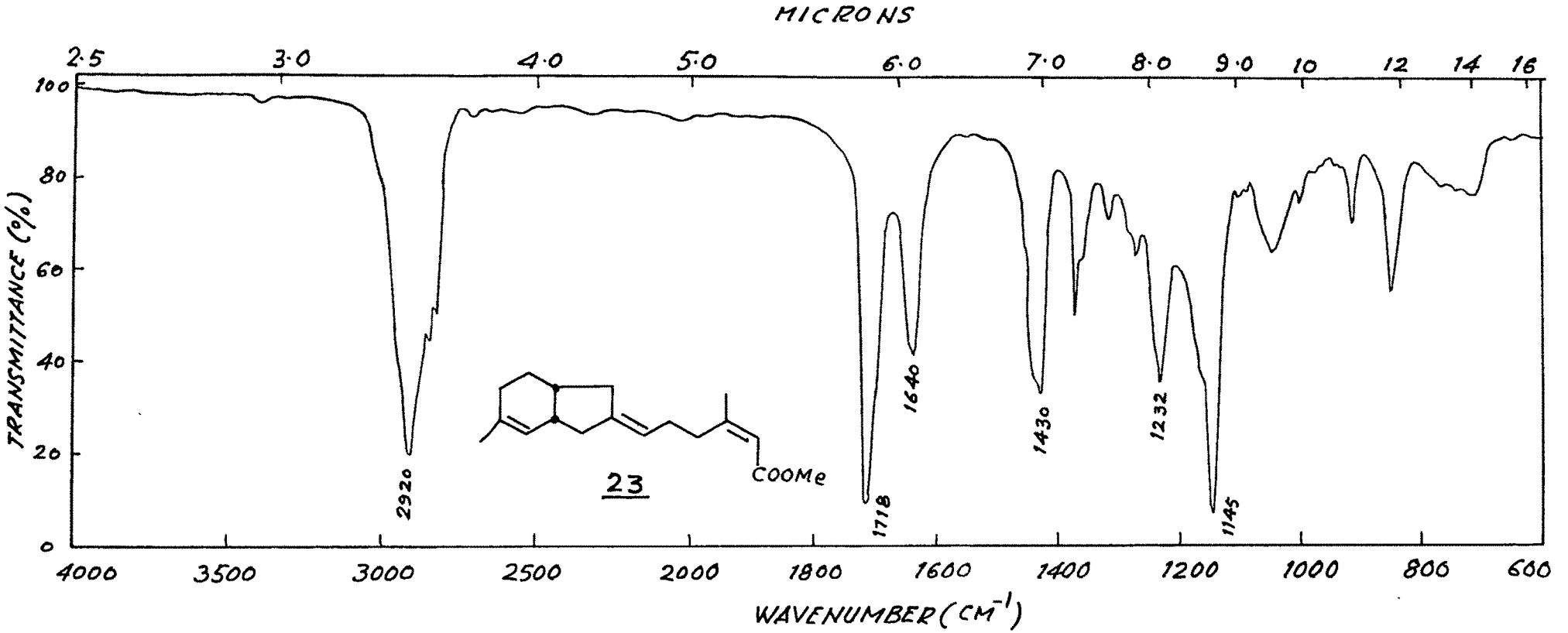


FIG. 13: IR SPECTRUM OF METHYL 7":9, 7":13-CIS-CYCLO-7-ETHYL-3,11-DIMETHYL-CIS-2,E-6,CIS-10-TRIDECATRIENOATE 23

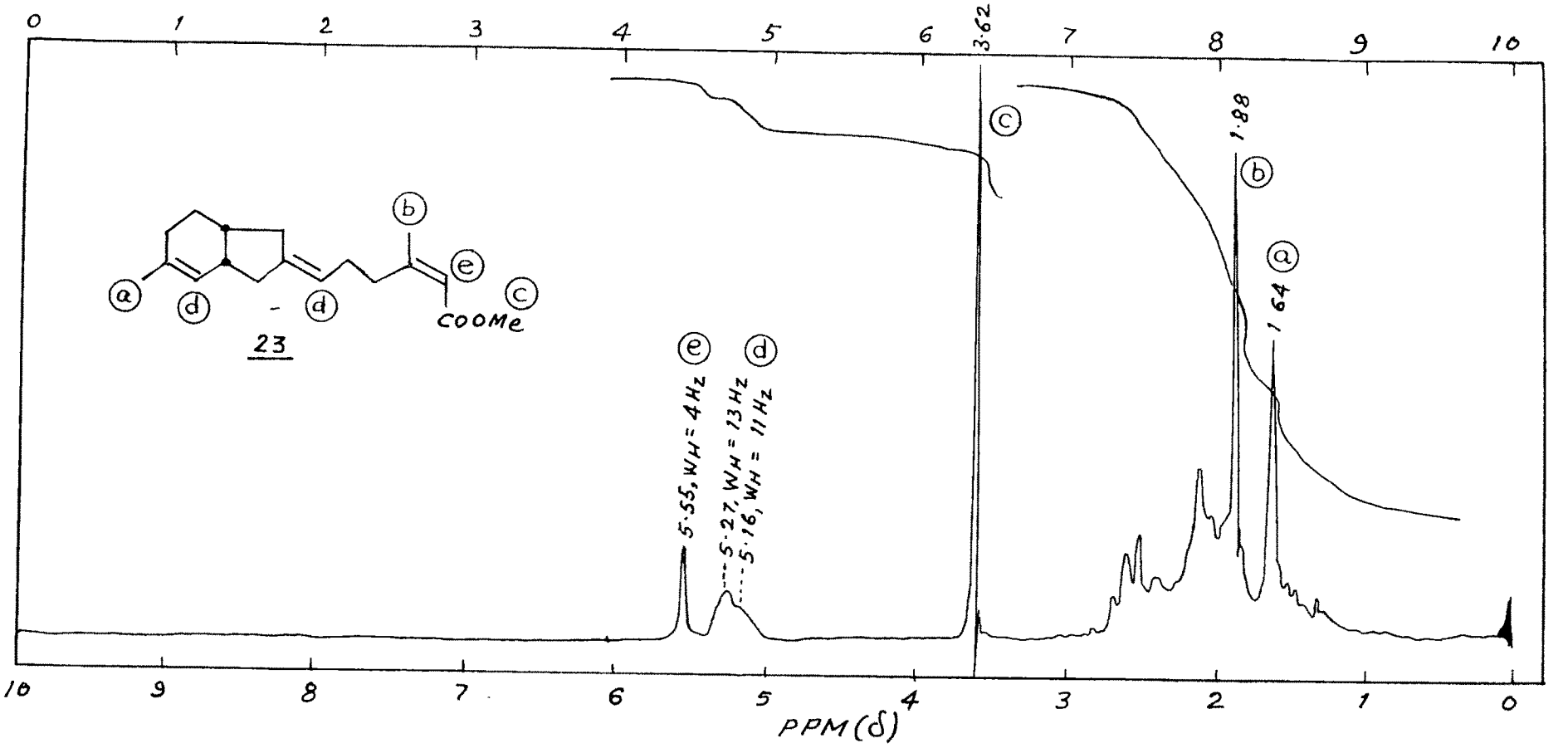


FIG. 14 : NMR SPECTRUM OF METHYL 7'':9, 7'':13-CIS-CYCLO-7-ETHYL-3,11-DIMETHYL-CIS-2,E-6,CIS-10-TRIDECATRIENOATE 23

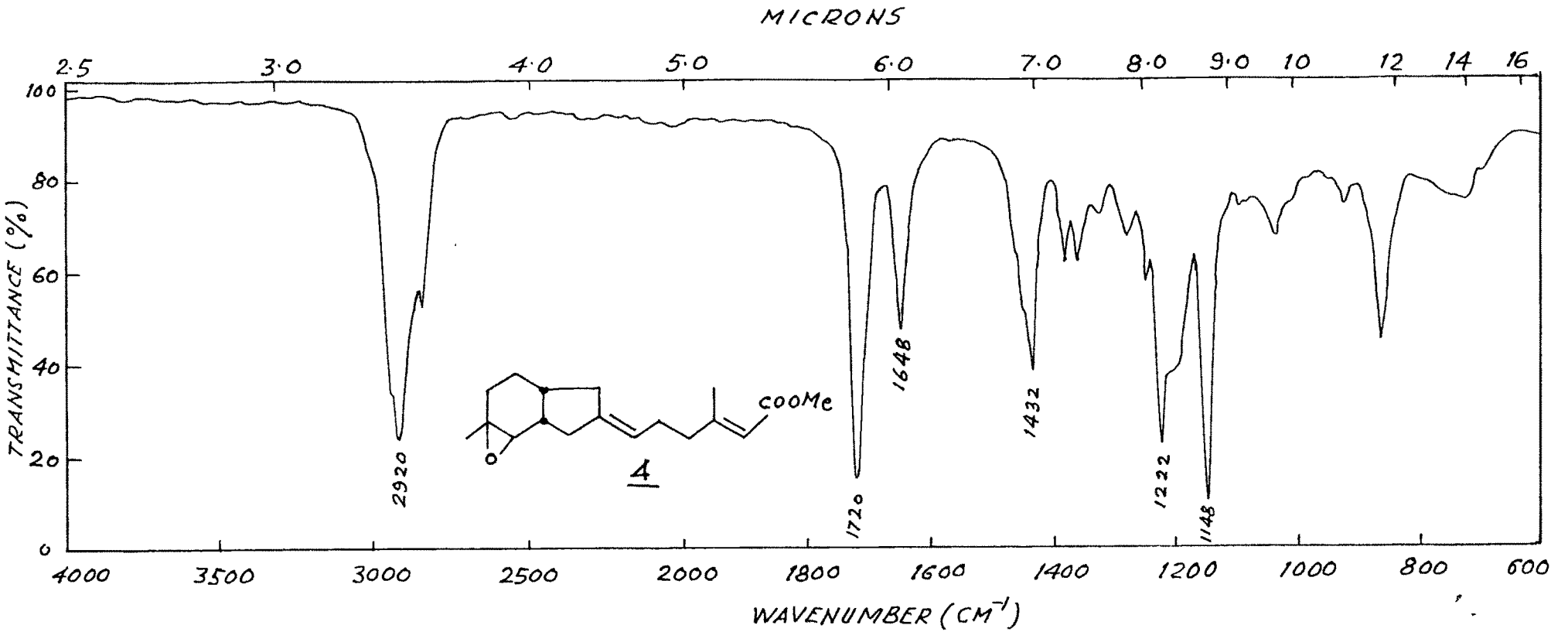


FIG. 15: IR SPECTRUM OF DL-METHYL 7'':9,7'':13-CIS-CYCLO-CIS-10,11-EPOXY-7-ETHYL-3,11-DIMETHYL-TRANS-2,E-6-TRIDECADIENOATE 4

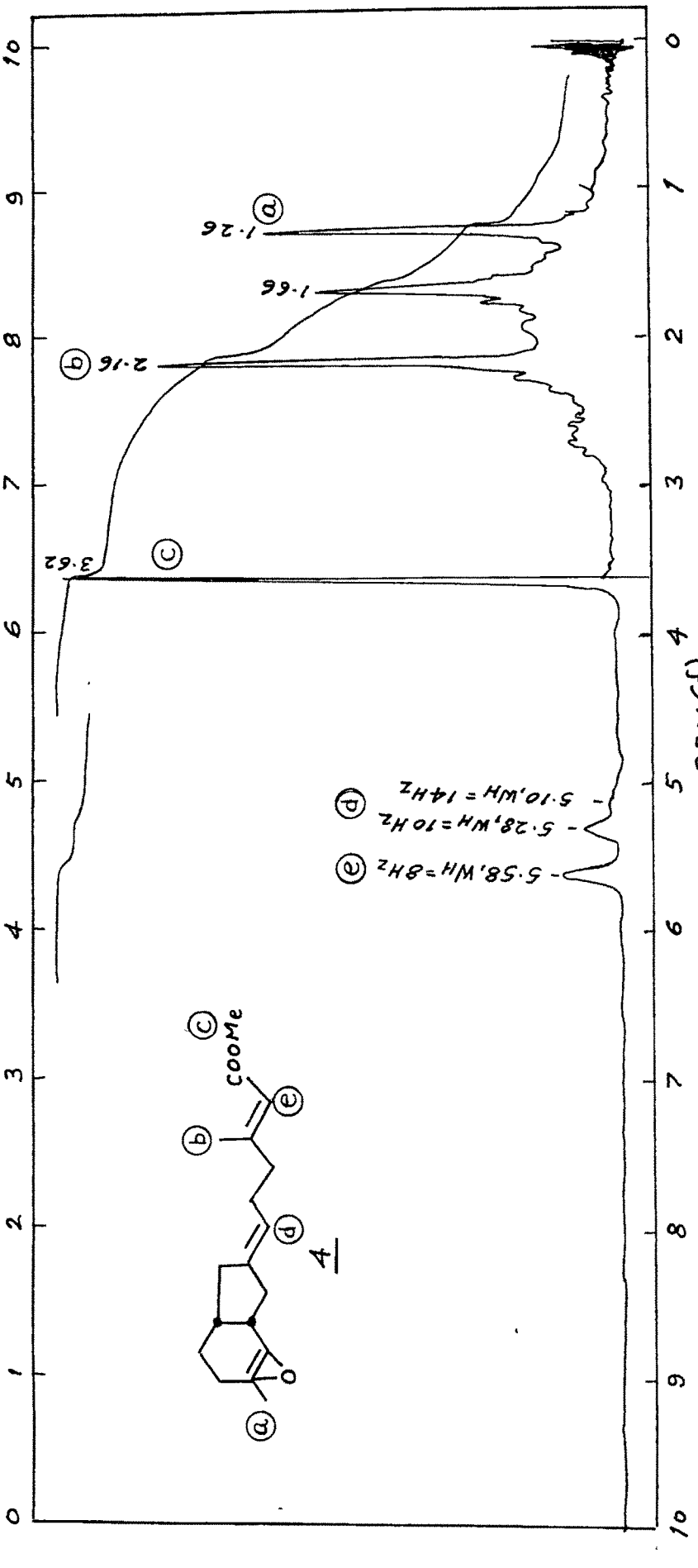


FIG.16: NMR SPECTRUM OF DL-METHYL 7":9, 7":13-CIS-CYCLO-CIS-10, 11-EPOXY-7-ETHYL-3, 11-DIMETHYL-TRANS-2, E-6-TRIDECADIENOATE 4

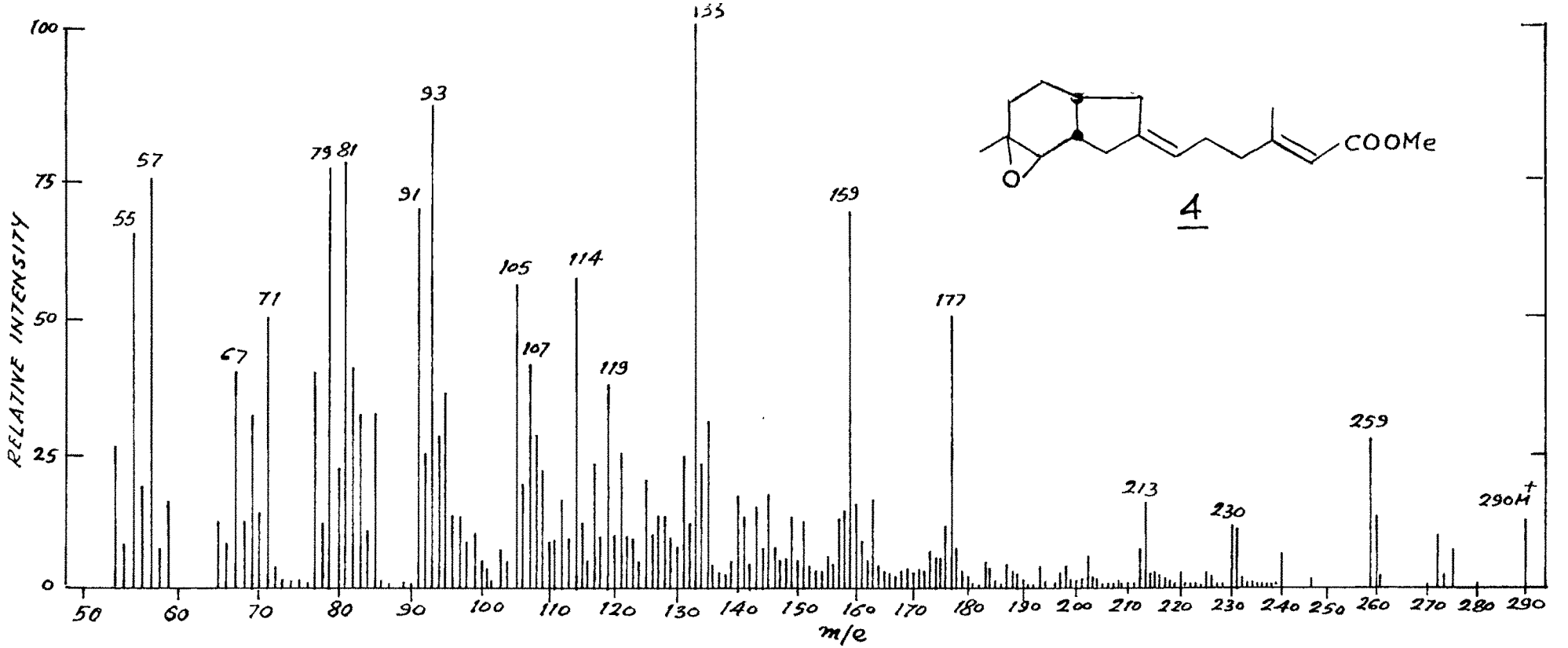


FIG. 16 A - MASS SPECTRUM OF DL-METHYL 7":9, 7":13-CIS-CYCLO-CIS-10,11-EPOXY-7-ETHYL-3,11-DIMETHYL-TRANS-2,6-TRIDECADIENOATE, 4

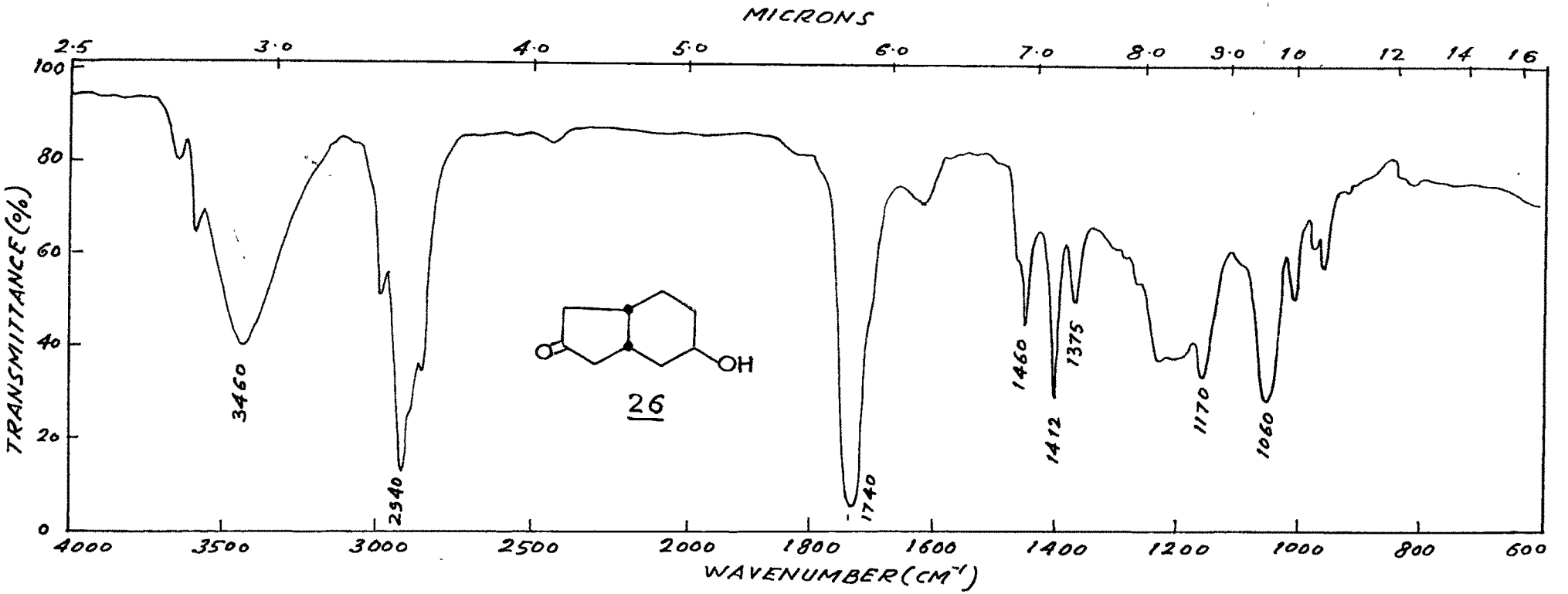


FIG. 17 - IR SPECTRUM OF CIS-BICYCLO (4,3,0) NONAN-3-OL-8-ONE 26

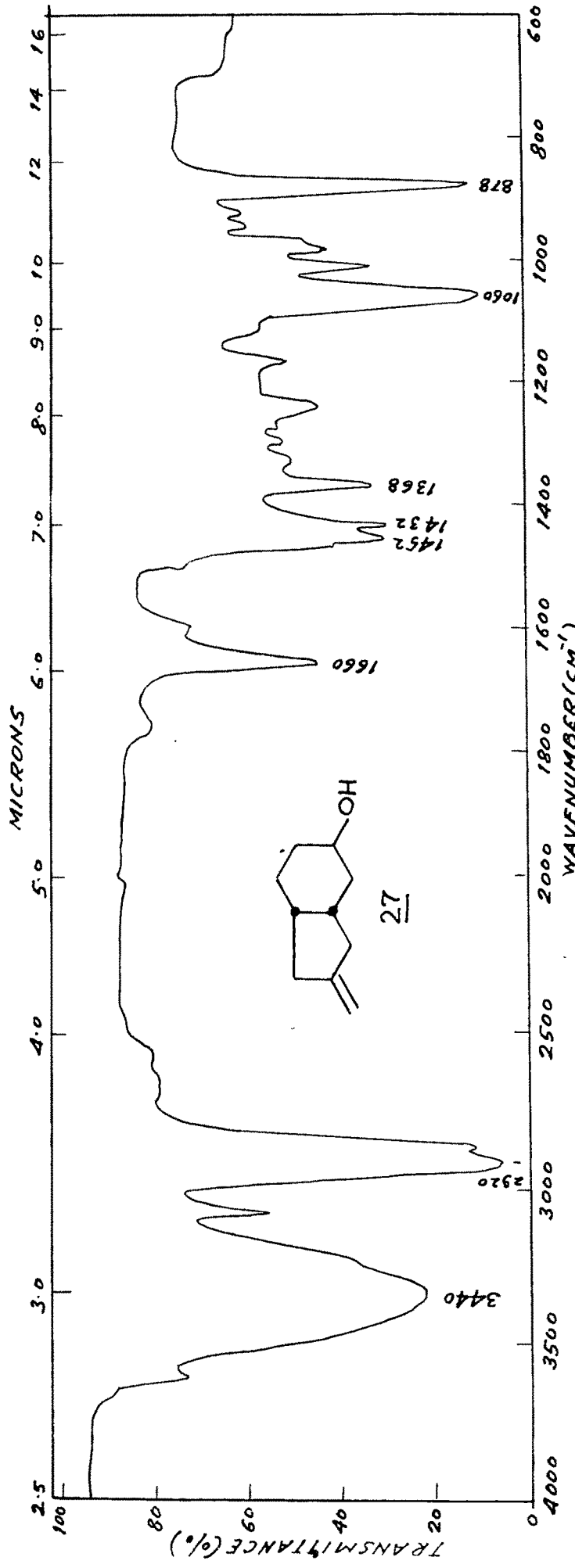


FIG. 18 - IR SPECTRUM OF 8-METHYLENE-CIS-BICYCLO(4,3,0)NONAN-3-OL 27

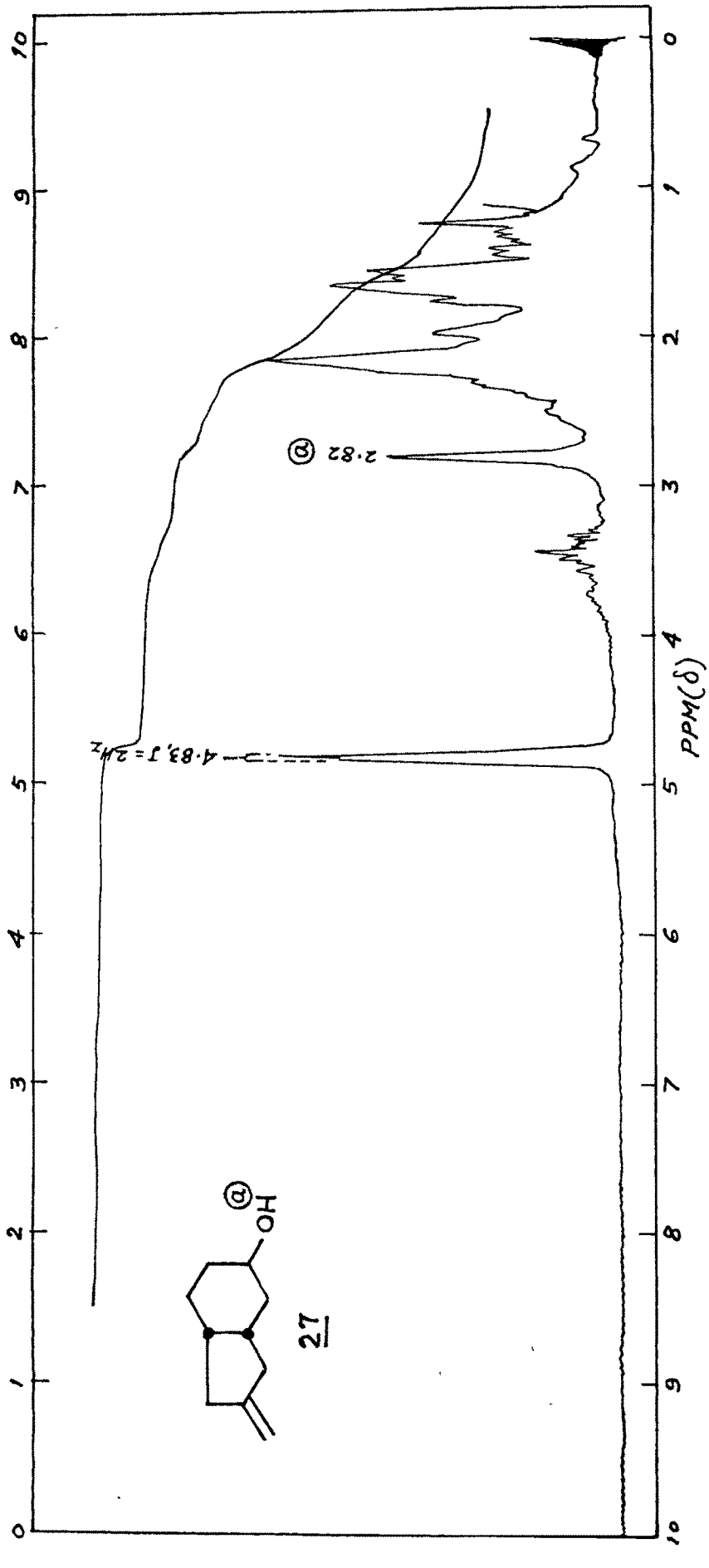


FIG. 19 - NMR SPECTRUM OF 8-METHYLENE- CIS-BICYCLO(4,3,0)NONAN-3-OL 27

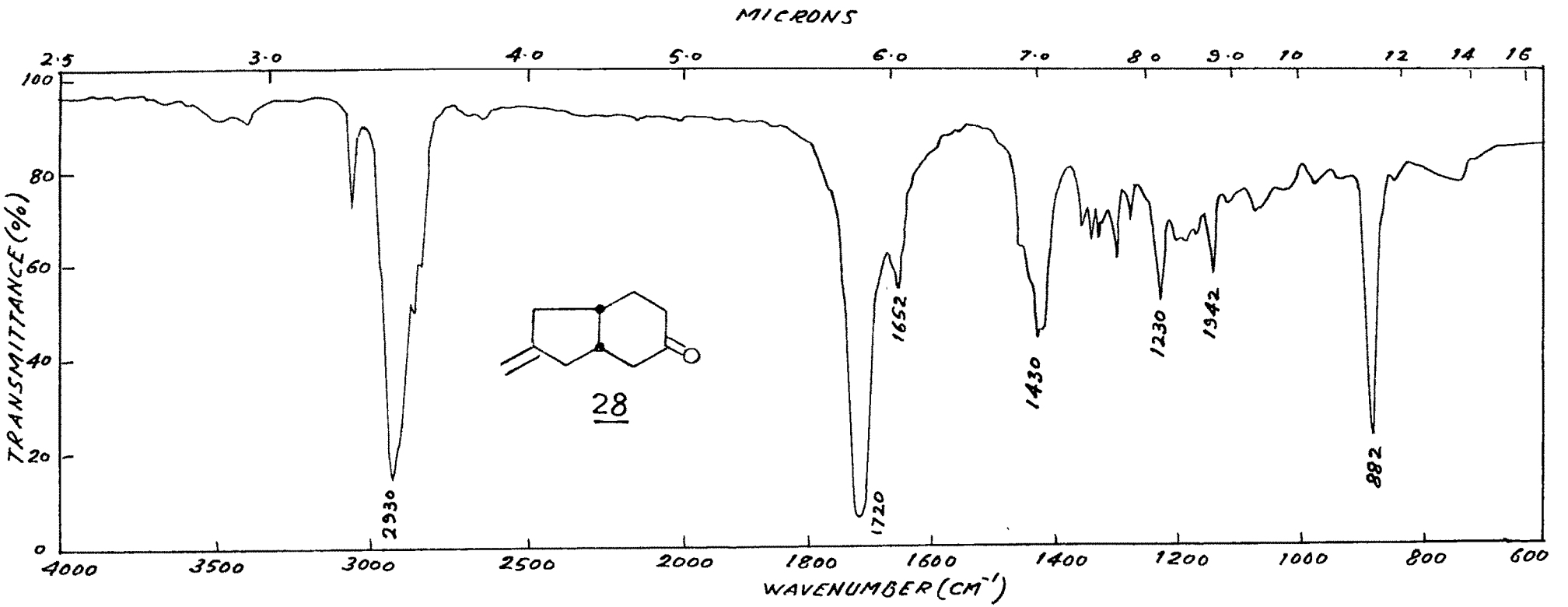


FIG. 20 - IR SPECTRUM OF 8-METHYLENE-CIS-BICYCLO(4,3,0)NONAN-3-ONE 28

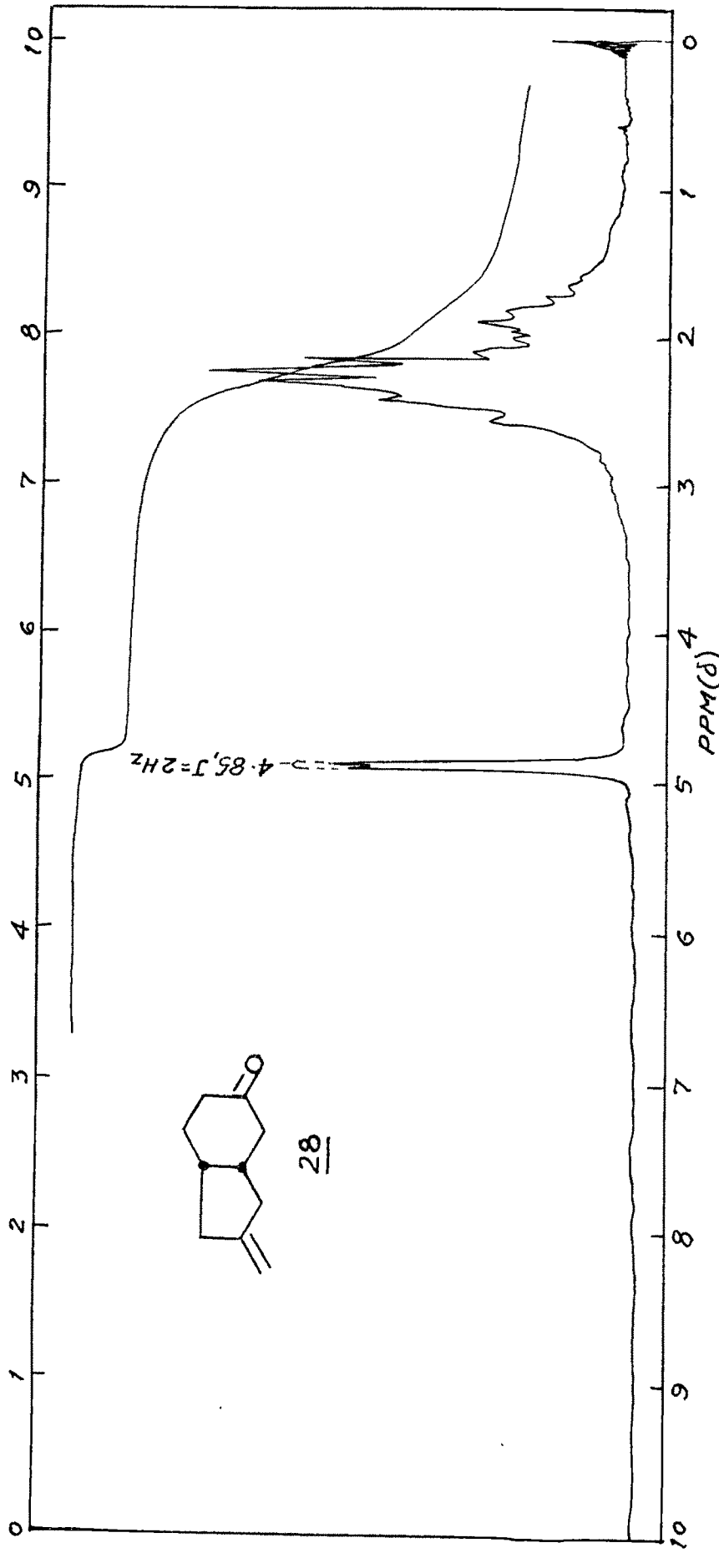


FIG. 21 - NMR SPECTRUM OF 8-METHYLENE-CIS-BICYCLO(4,3,0)NONAN-3-ONE 28

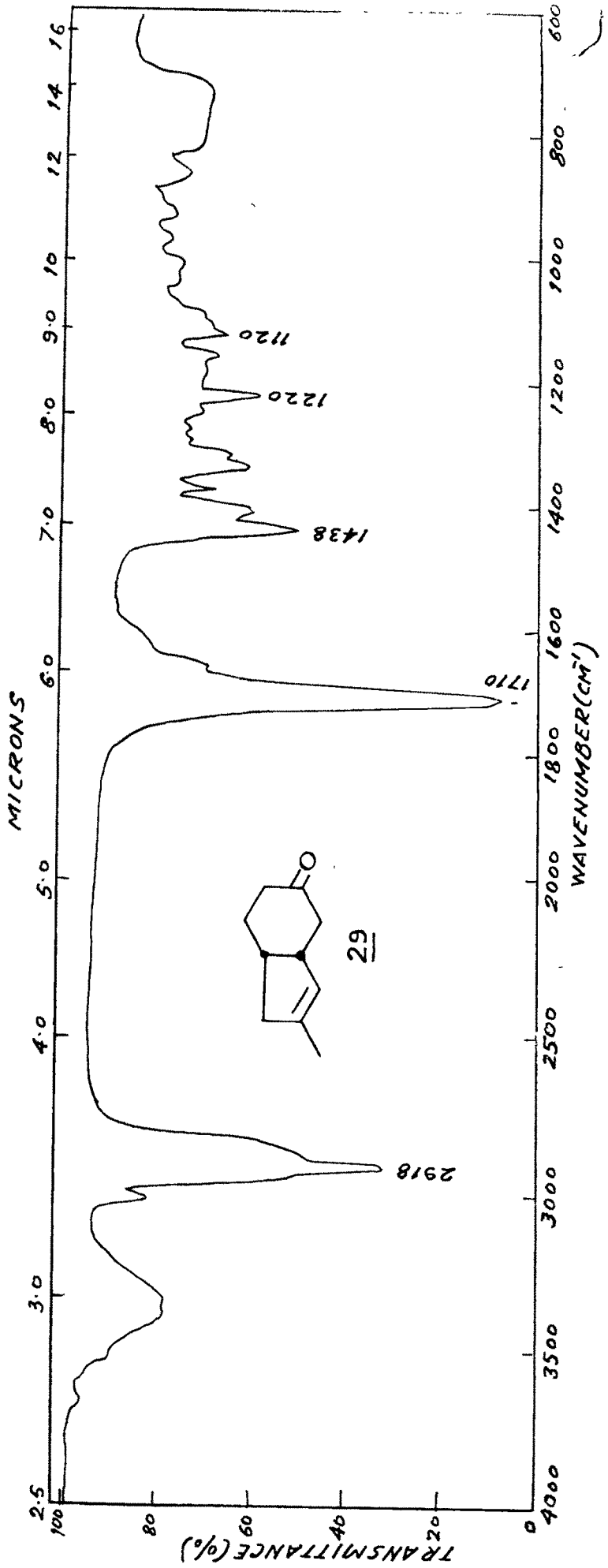


FIG. 22 - IR SPECTRUM OF 8-METHYL-CIS-BICYCLO(4,3,0)NON-8-EN-3-ONE 29

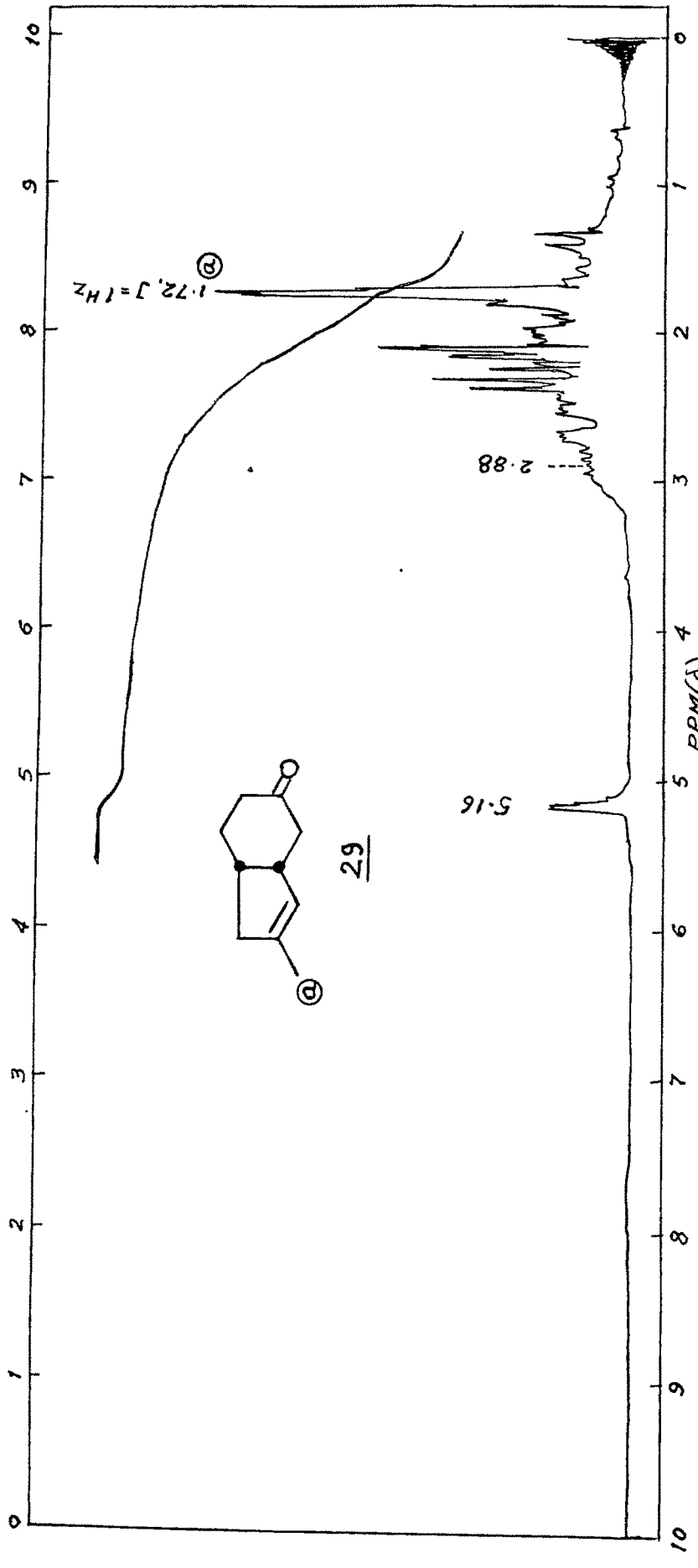


FIG. 23- NMR SPECTRUM OF 8-METHYL-CIS-BICYCLO (4,3,0) NON-8-EN-3-ONE 29

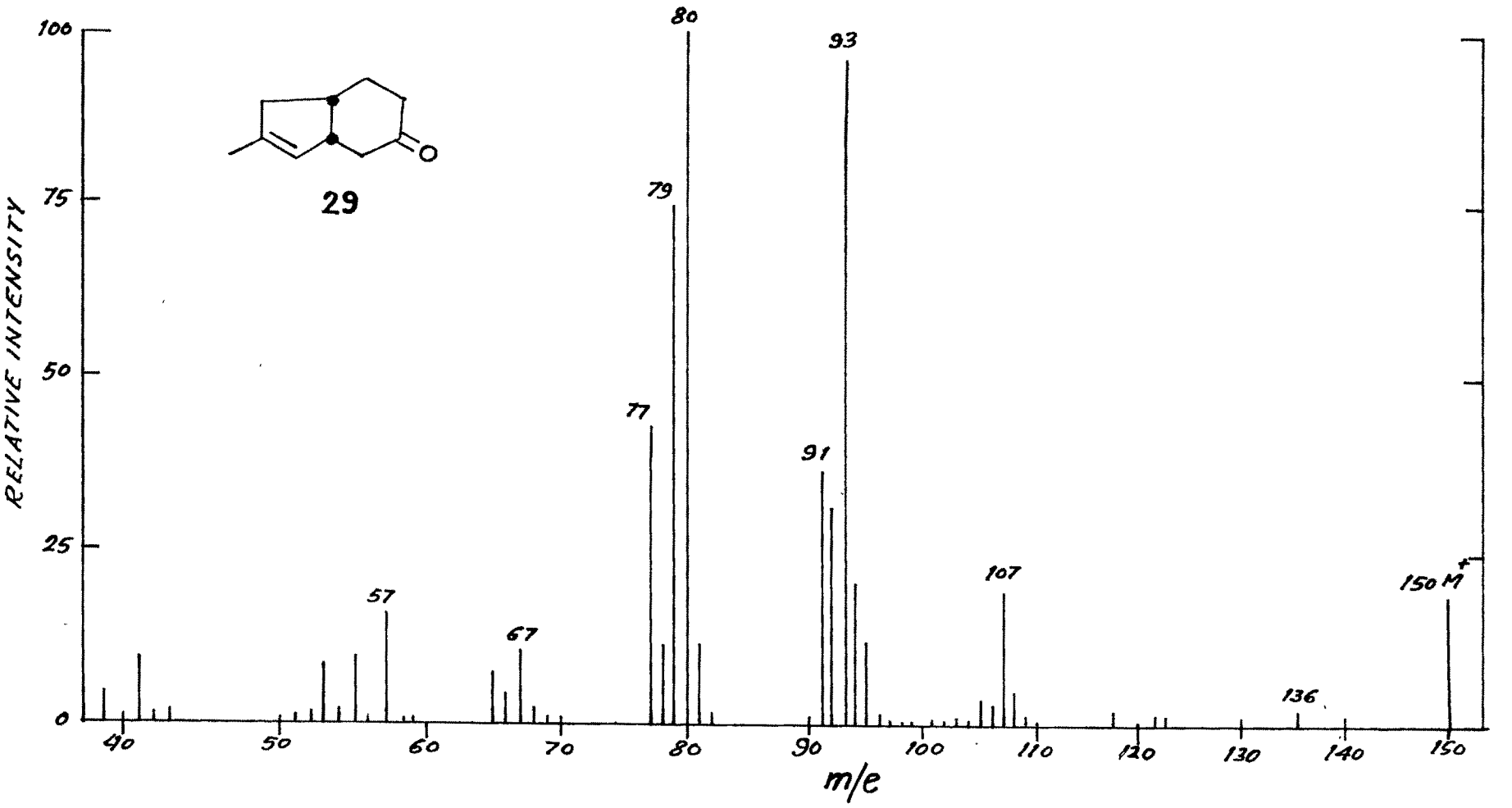


FIG. 23 A - MASS SPECTRUM OF 8-METHYL-CIS-BICYCLO(4,3,0)NON-8-EN-3-ONE, 29

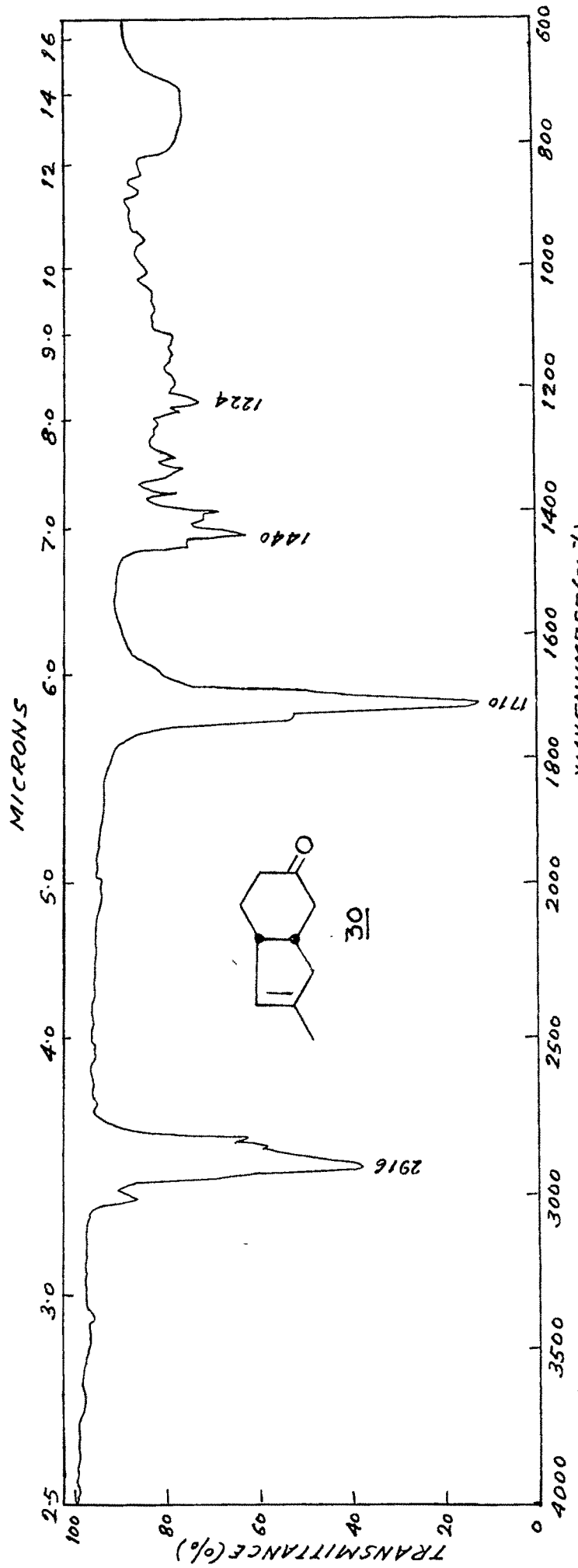


FIG. 24 - IR SPECTRUM OF 8-METHYL-CIS-BICYCLO (4,3,0) NON-7-EN-3-ONE 30

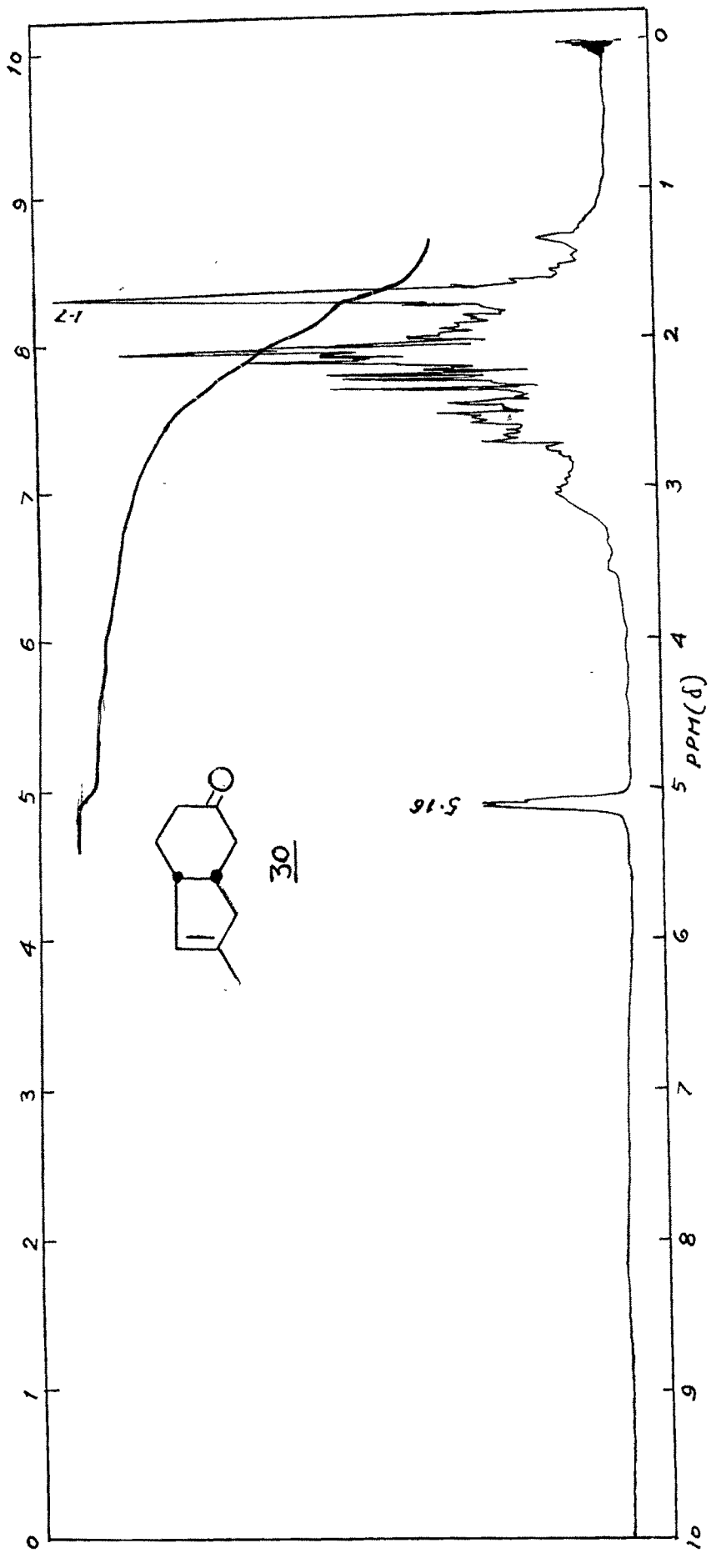


FIG. 25 - NMR SPECTRUM OF 8-METHYL-CIS-BICYCLO(4,3,0) NON-7-EN-3-ONE 30

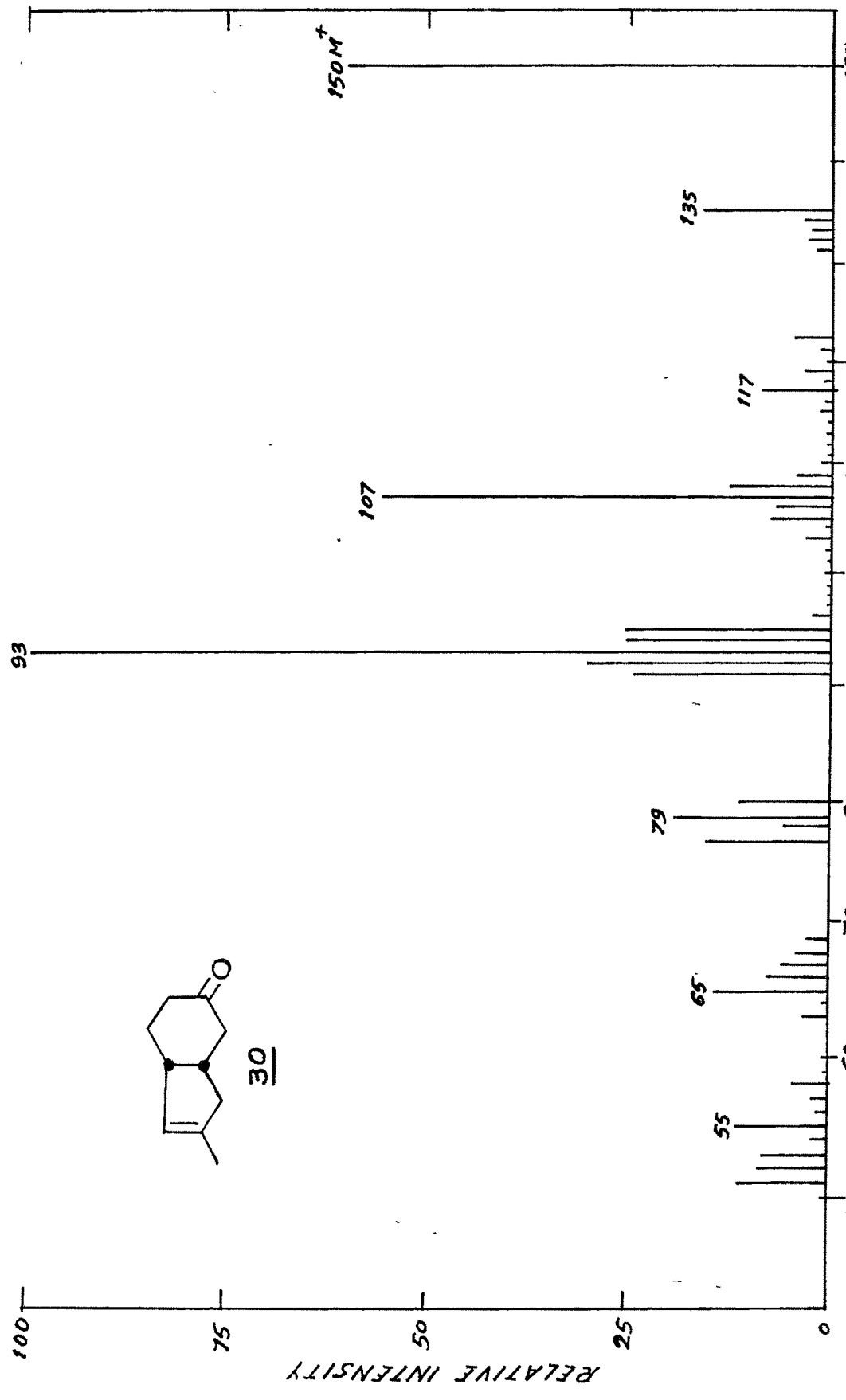


FIG. 25A - MASS SPECTRUM OF 8-METHYL-CIS-BICYCLO(4,3,0)NON-7-EN-3-ONE; 30

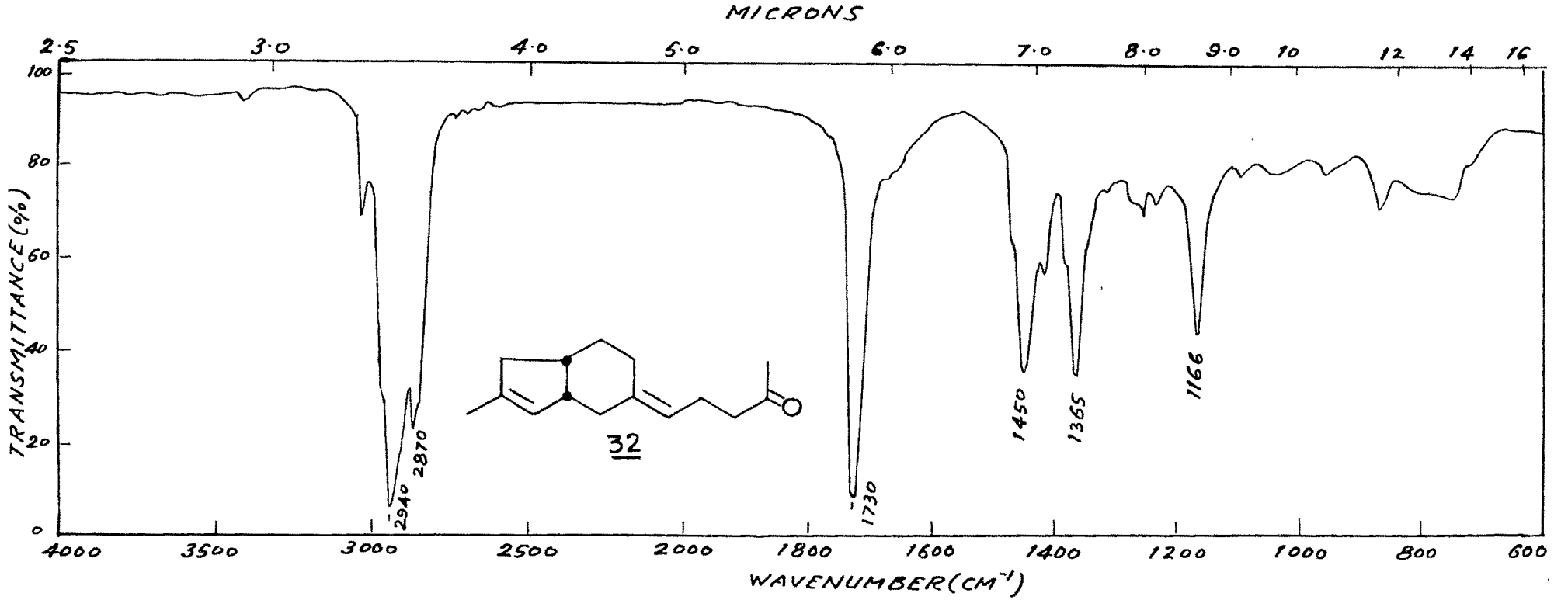


FIG. 26 - IR SPECTRUM OF 6":12, 8:12-CIS-CYCLO-10-METHYL-6-ETHYL-§-5, CIS-9-DODECADIENE-2-ONE 32

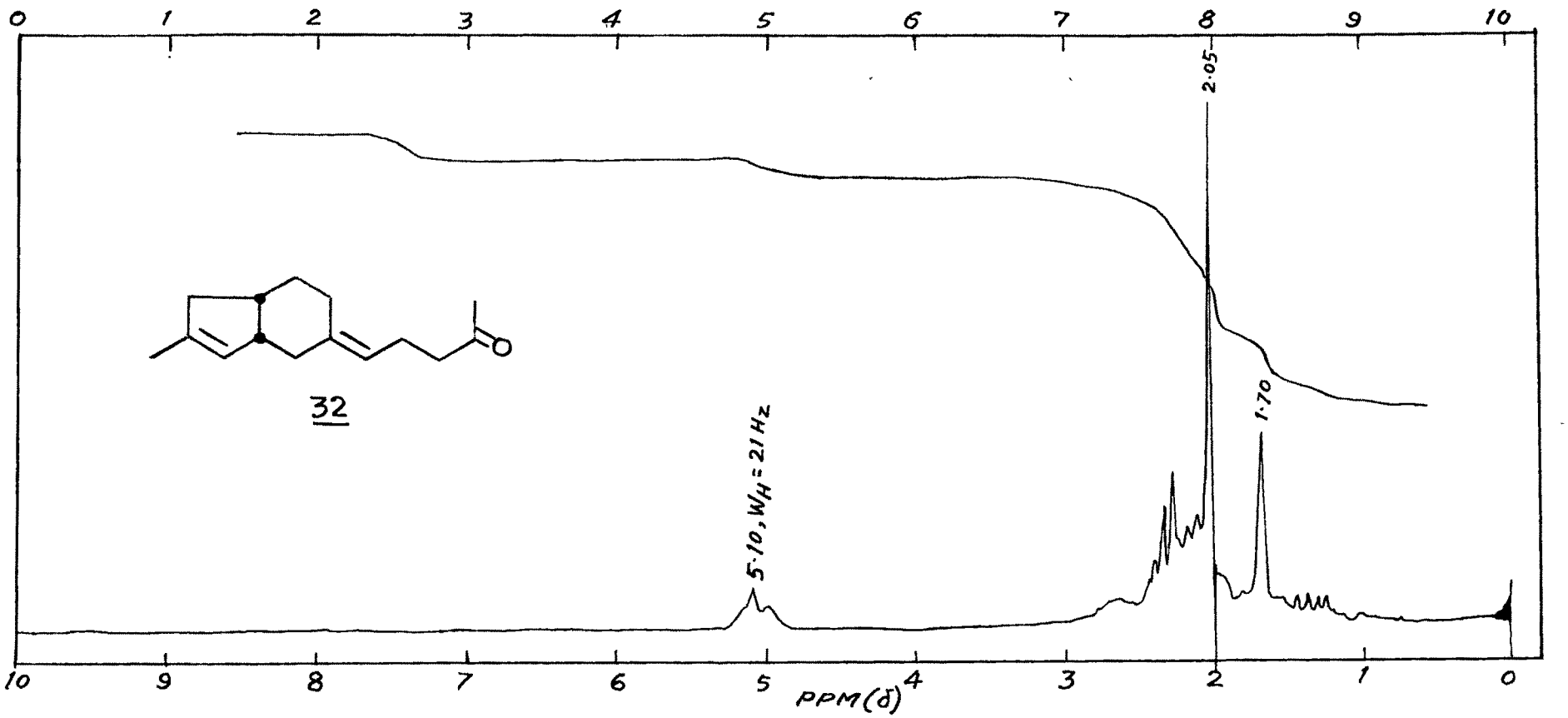


FIG. 27 - NMR SPECTRUM OF 6":12, 8:12 - CIS - CYCLO - 10 - METHYL - 6 - ETHYL - E - 5, CIS - 9 - DODECADIENE - 2 - ONE 32

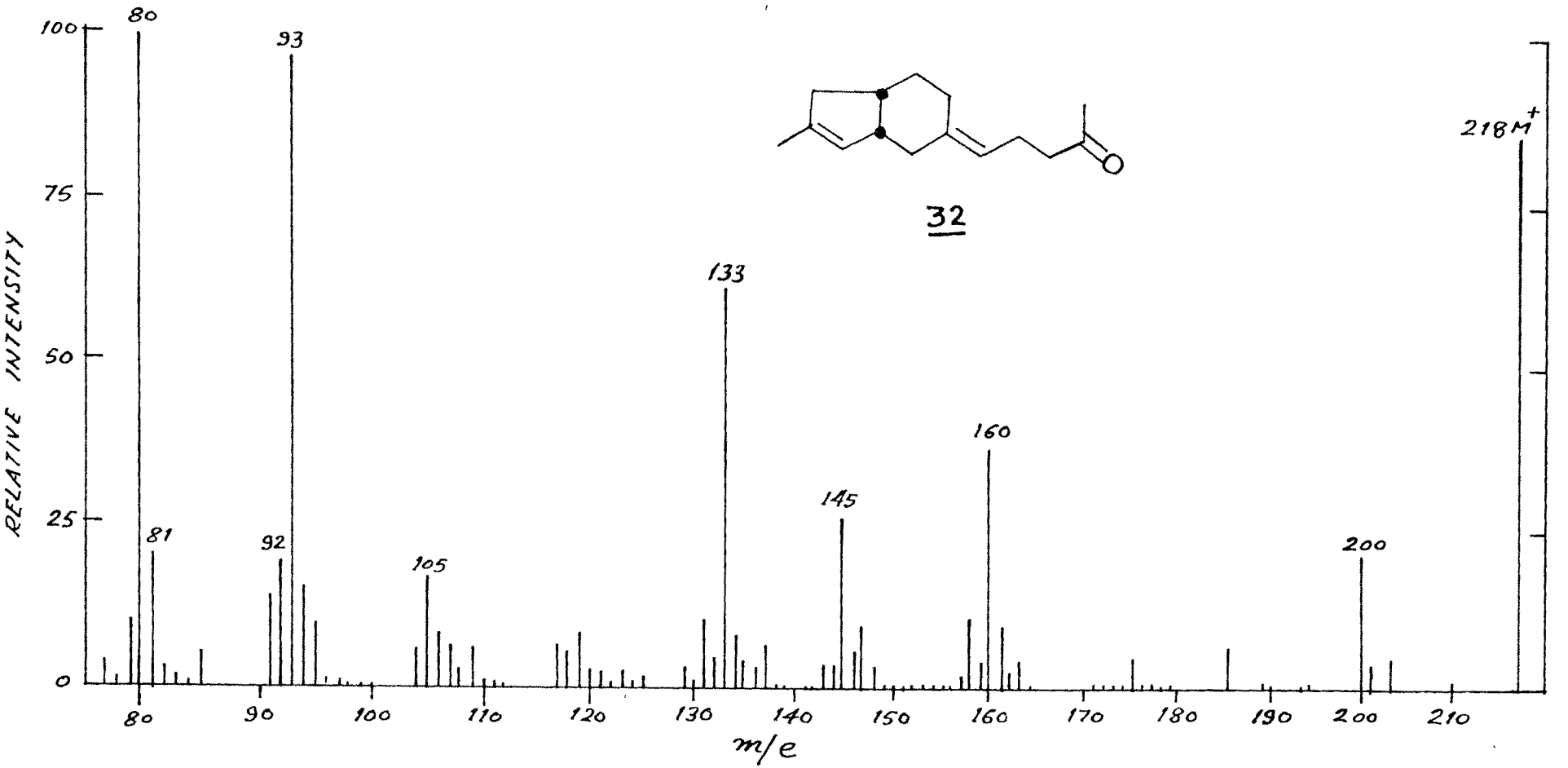


FIG. 27A - MASS SPECTRUM OF 6'':12,8:12-CIS-CYCLO-10-METHYL-6-ETHYL-ξ-5;CIS-9-DODECADIENE-2-ONE; 32

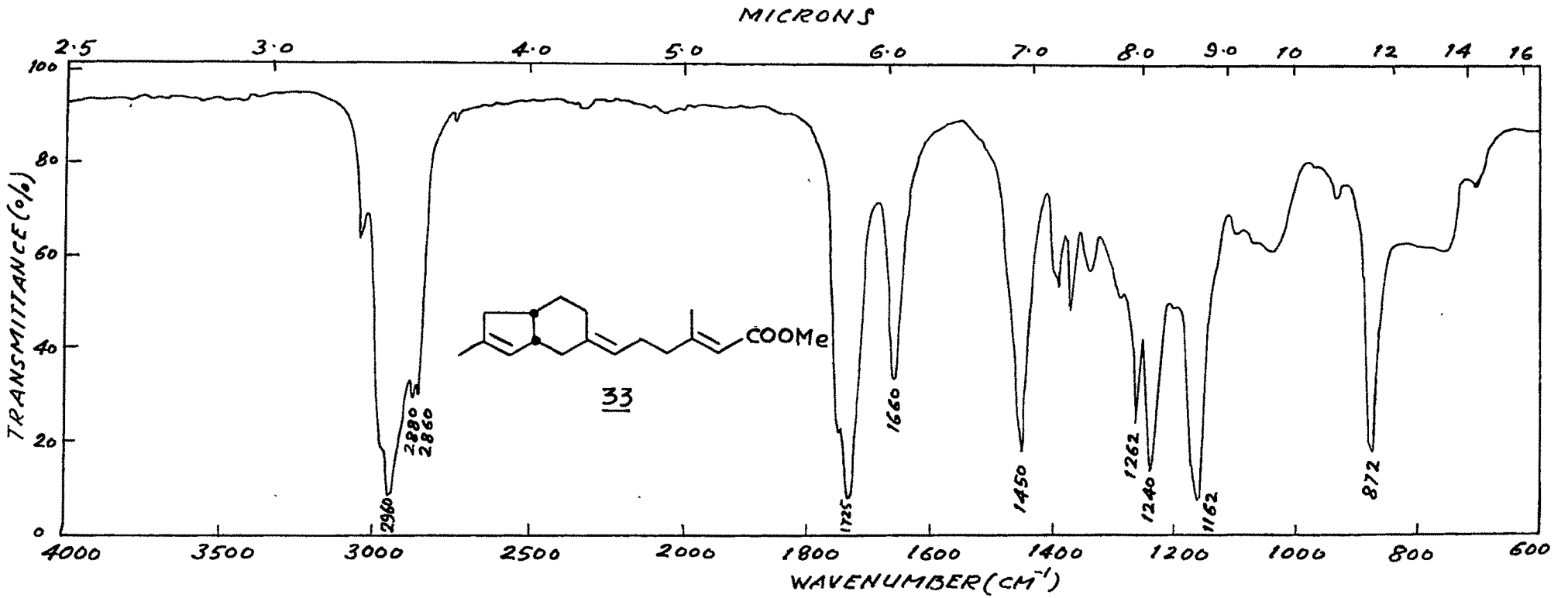


FIG.28 - IR SPECTRUM OF METHYL 7"13,9:13 - CIS - CYCLO-7-ETHYL-3,11-DIMETHYL-TRANS-2,E-6,CIS-10-TRIDECATRIENOATE 33

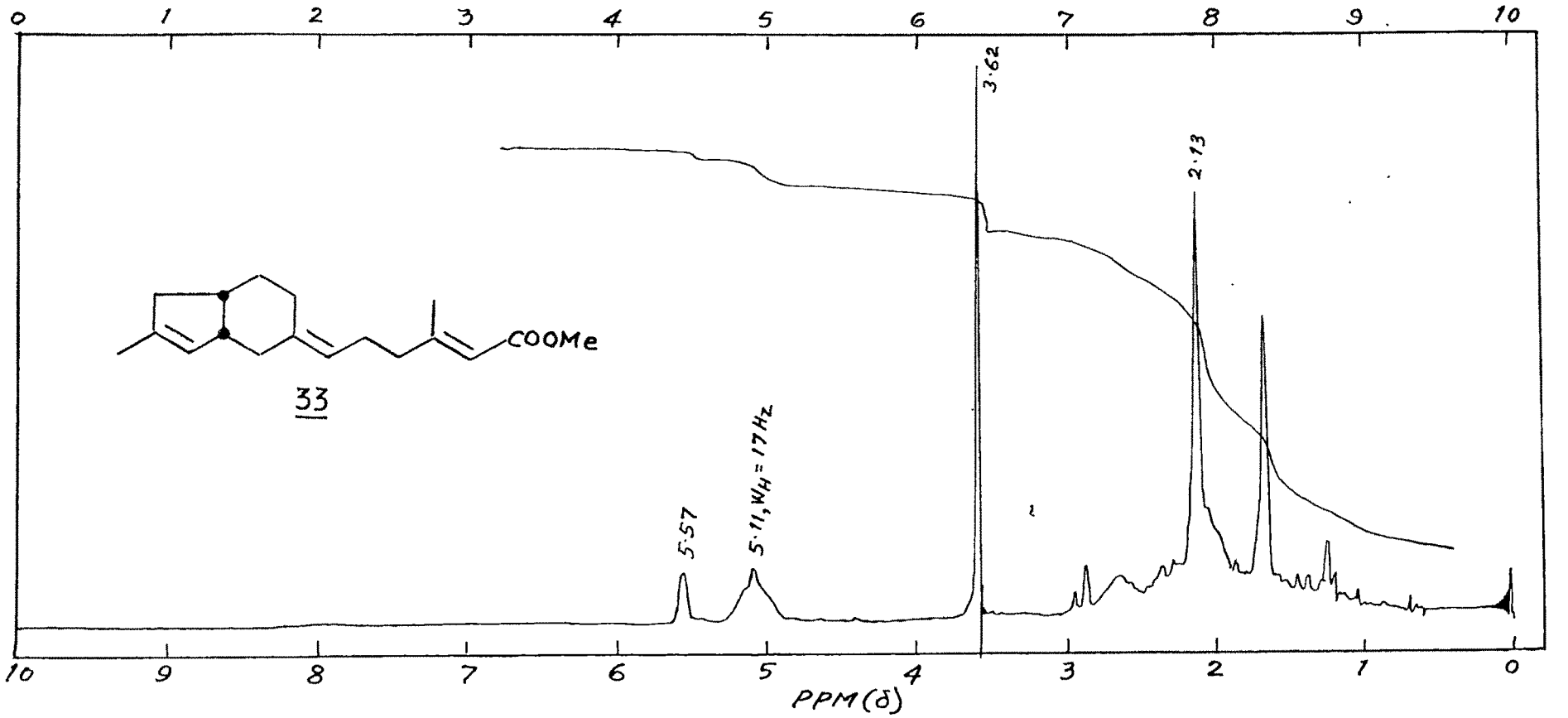


FIG. 29 - NMR SPECTRUM OF METHYL 7'':13,9:13 - CIS - CYCLO-7-ETHYL-3,11-DIMETHYL-TRANS-2, E-6, CIS-10-TRIDECATRIENOATE 33

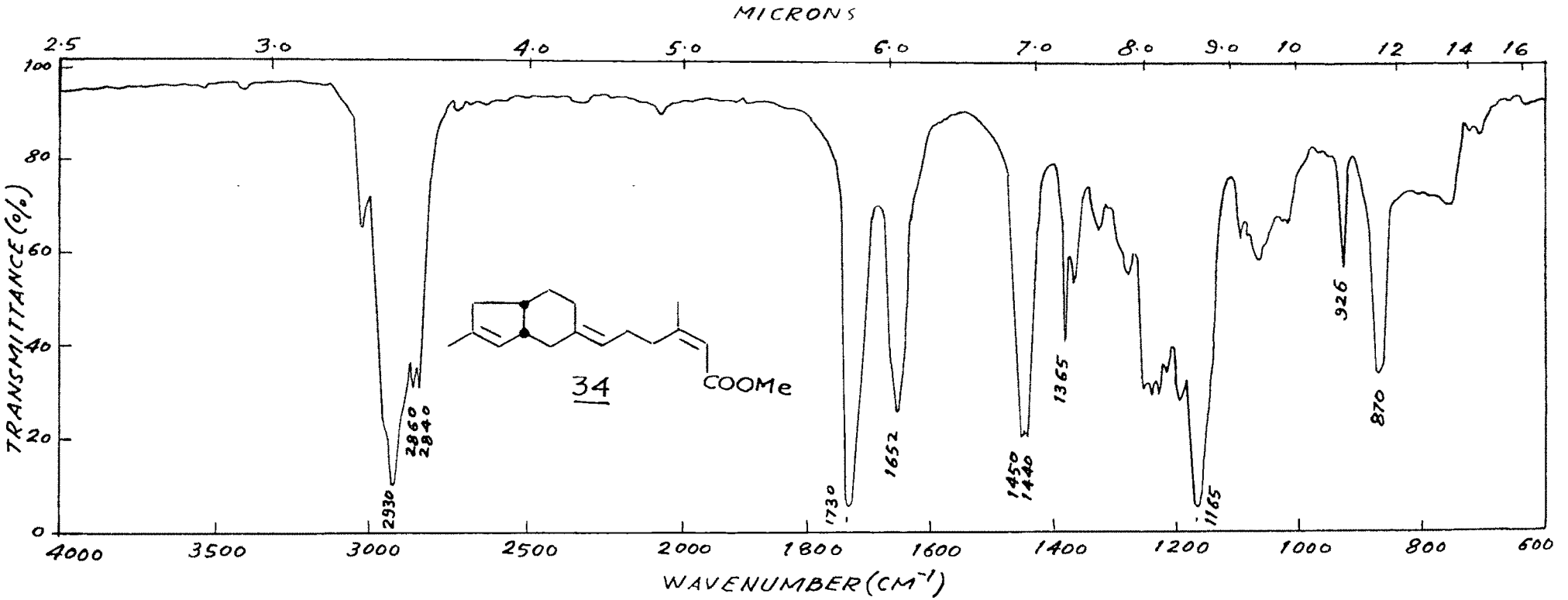


FIG.30 - IR SPECTRUM OF 7'':13,9:13-CIS-CYCLO-7-ETHYL-3,11-DIMETHYL-CIS-2,E-6,CIS-10-TRIDECATRIENOATE 34

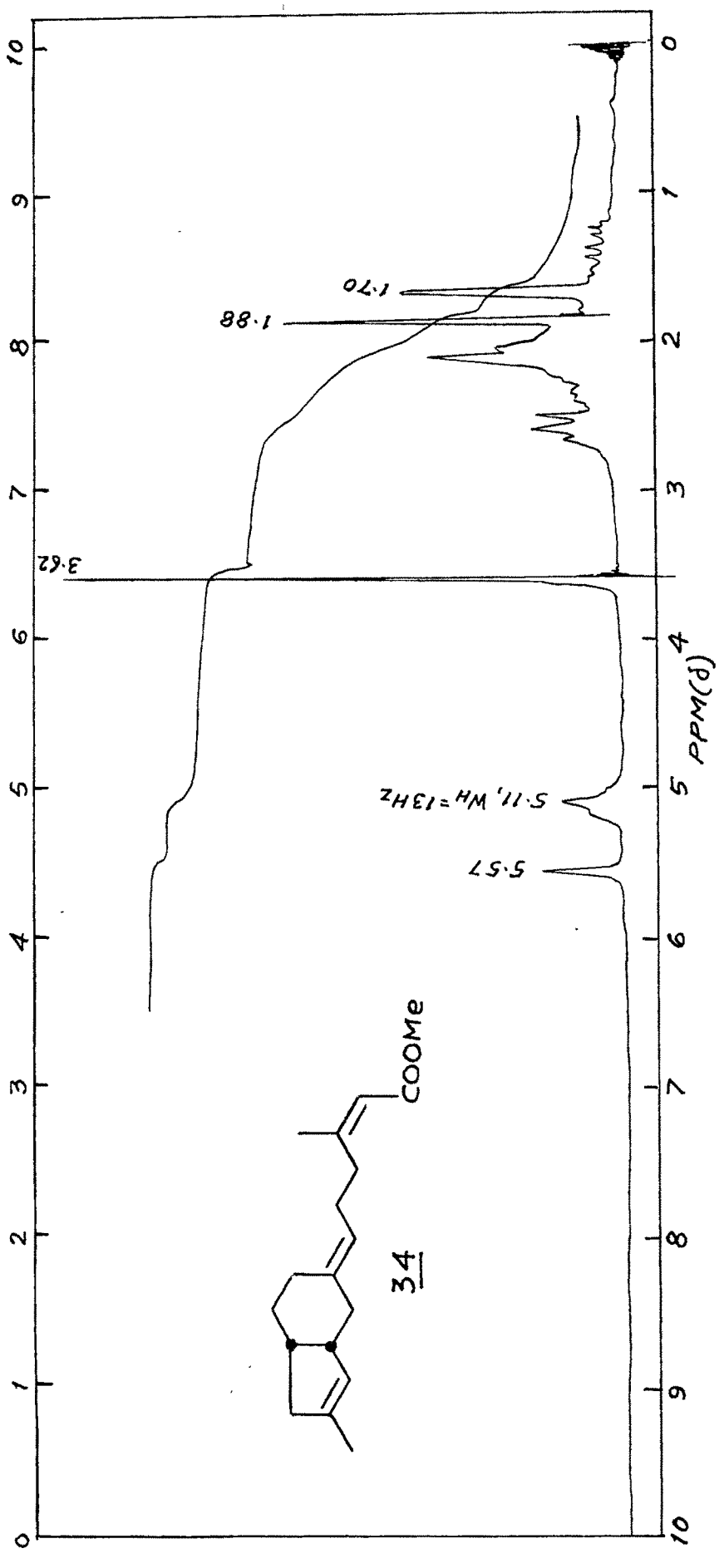


FIG. 31 - NMR SPECTRUM OF "7:13,9:13-CIS-CYCLO-7-ETHYL-3,11-DIMETHYL-CIS-2,E-6, CIS-10-TRIDECATRIENOATE 34

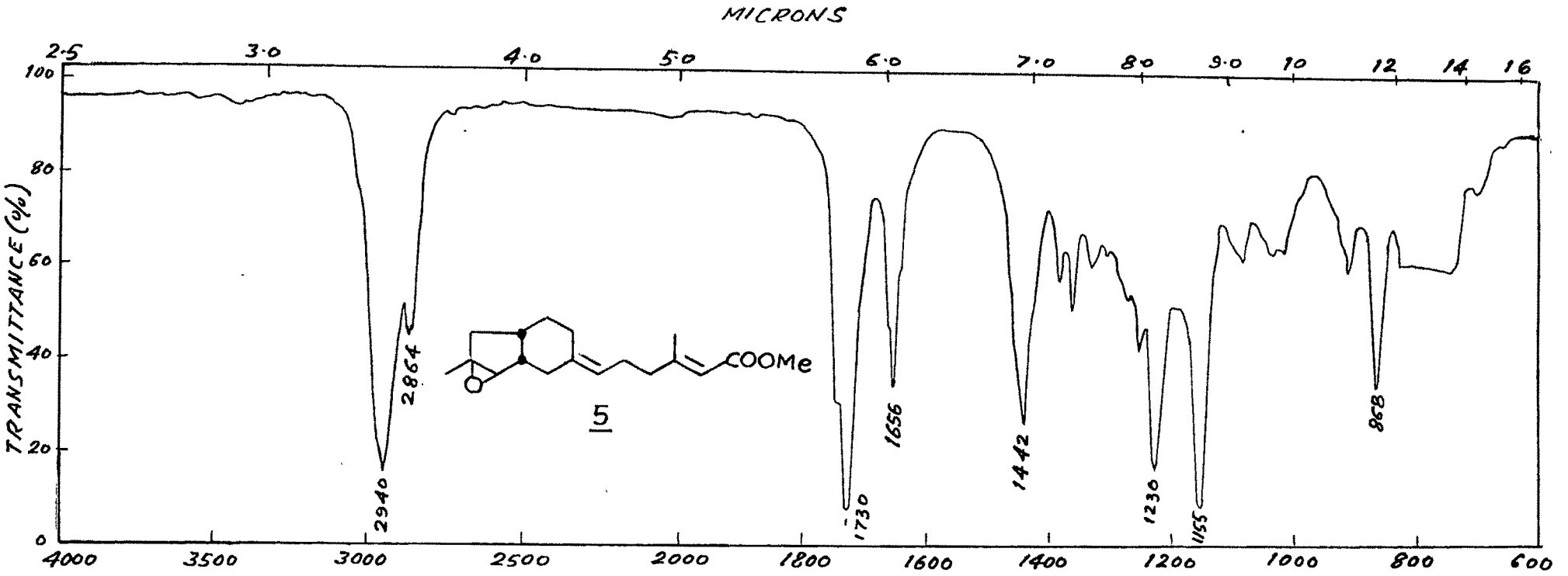


FIG. 32 - IR SPECTRUM OF DL-METHYL 7:13, 9:13-CIS-CYCLO-CIS-10,11-EPOXY-7-ETHYL-3,11-DIMETHYL-TRANS-2,E-6-TRIDECADIENOATE 5

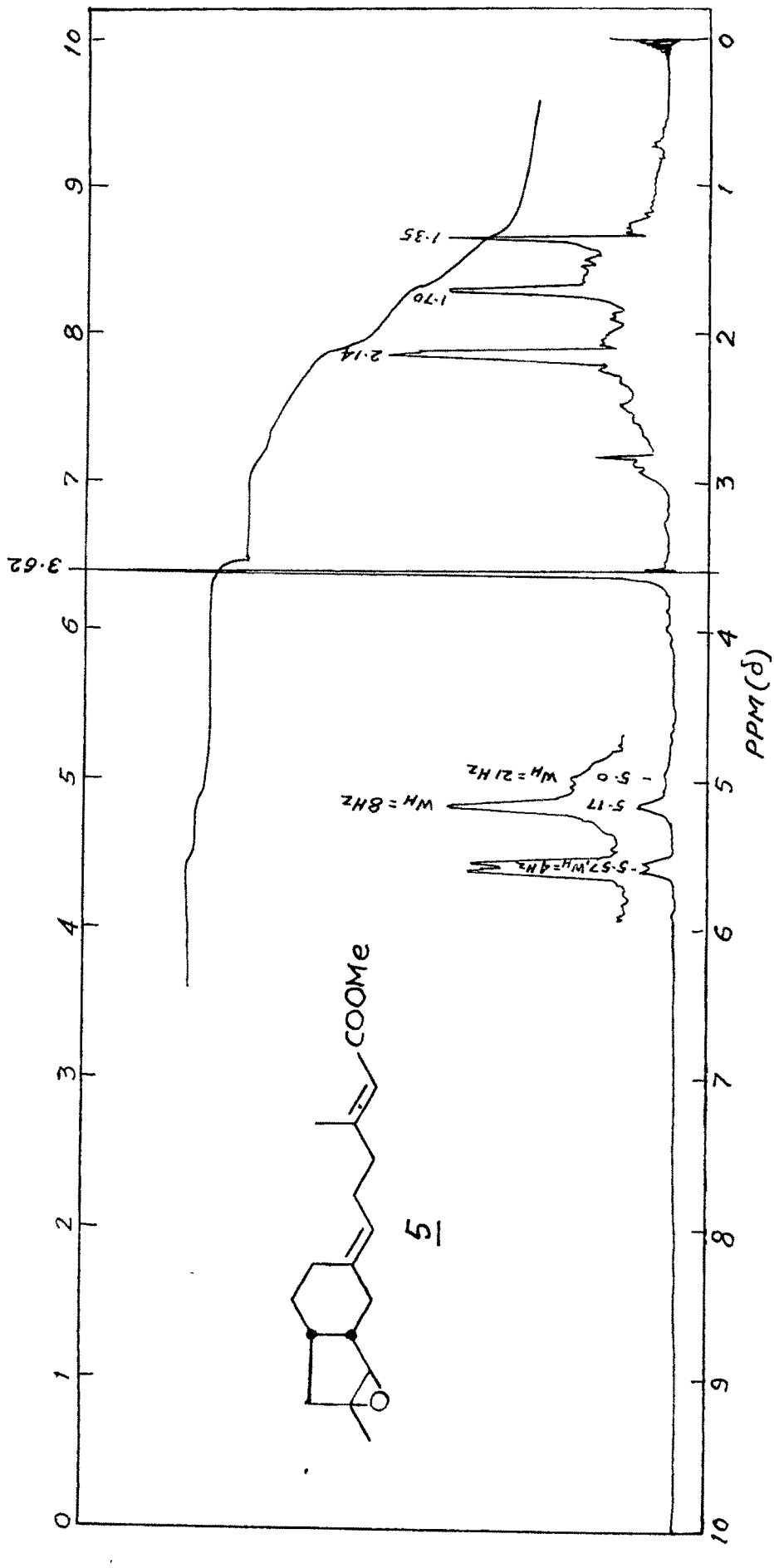


FIG. 33- NMR SPECTRUM OF DL-METHYL 7':13, 9:13-CIS-CYCLO-CIS-10,11-EPOXY-7-ETHYL-3,11-DIMETHYL-TRANS-2,E-6-TRIDECADIENOATE 5

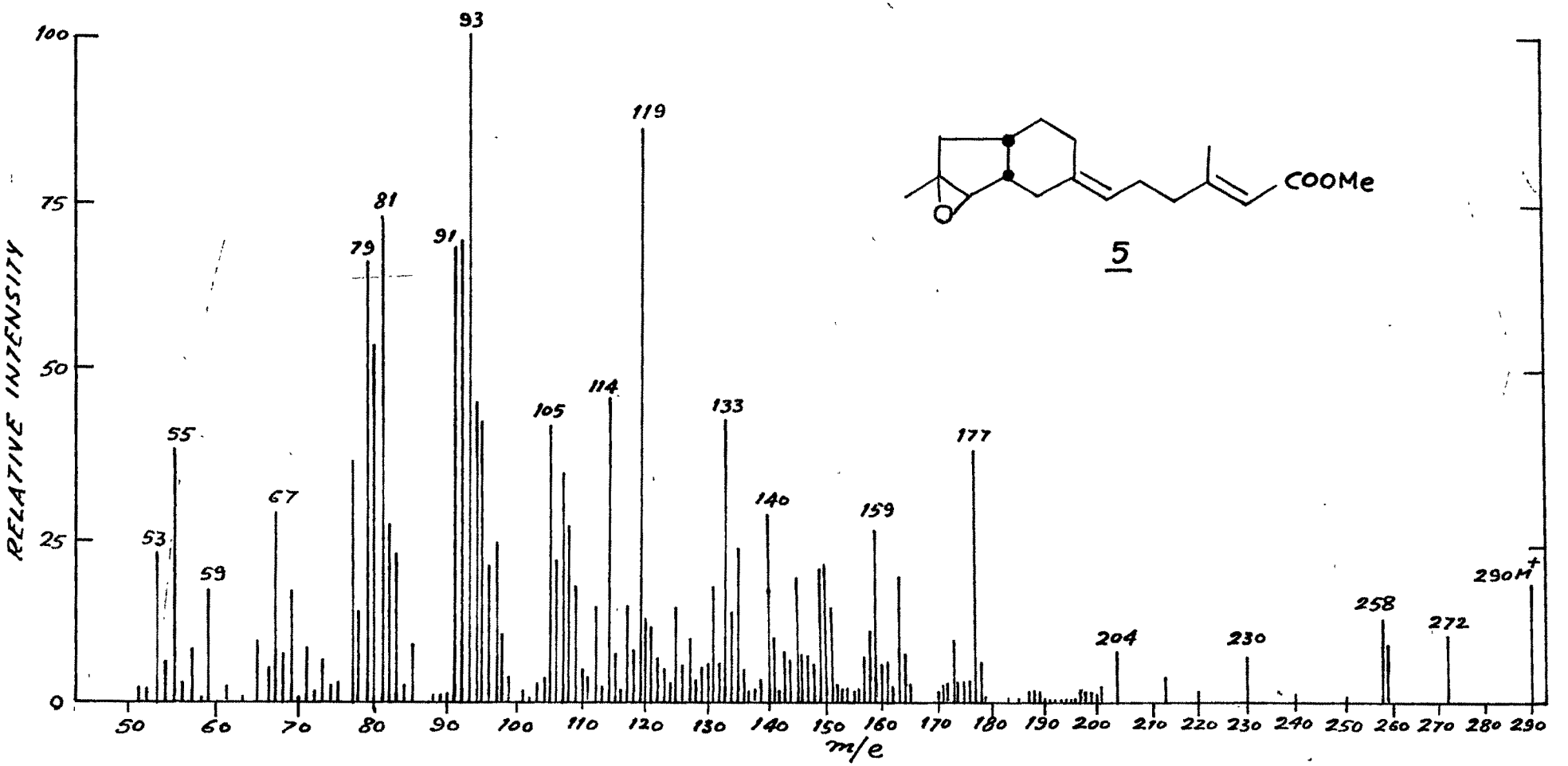


FIG. 33 A - MASS SPECTRUM OF DL-METHYL 7":13, 9:13 - CIS - CYCLO - CIS - 10,11 - EPOXY - 7 - ETHYL - 3,11 - DIMETHYL - TRANS - 2, E - 6 - TRIDECADIENOATE. 5

SECTION–II

CIS — PERHYDROINDANE ANALOGUE OF CECROPIA JUVENILE HORMONE (Part - II)

dl - Methyl 3" : 7", 5 : 7" - cis - cyclo - 10, 11 - epoxy - 11 - Methyl - 3, 7 - diethyl - 2, 7 - dodecadienoate.

cis-PERHYDROINDANE ANALOGUE OF CECROPIA JUVENILE HORMONE (Part II)

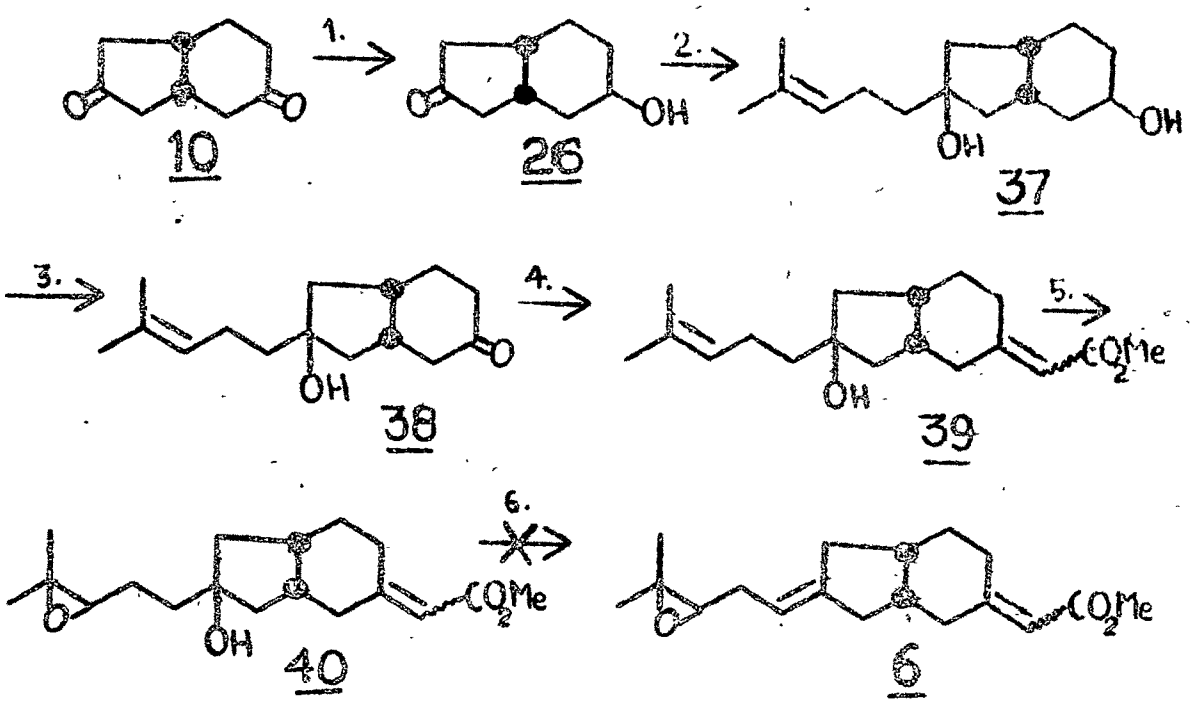
INTRODUCTION

The present section represents, the efforts directed towards the synthesis of dl-methyl 3" : 7", 5 : 7" -cis-cyclo-10,11-epoxy-11-methyl-3,7-diethyl-2,7-dodecadienoate 6[+]. The cis-perhydroindane ring of 6 is formed from 3" : 7" and 5 : 7" carbon atoms (Fig. 2). The regidity of the molecule caused by the presence of cis-perhydroindane ring has been further increased by shifting the double from 6,7 to 7,8 positions.

RESULTS AND DISCUSSION

For the synthesis of 6, the scheme followed is depicted in Fig. 8. The starting diketone 10 was converted to the hydroxy-ketone 26 with $NaBH_4/EtOH$[24,25], and thence to the Grignard addition product 37 with 4-methyl-3-pentenyl bromide[29] — magnesium-ether.[30] Chromium trioxide-pyridine[31] oxidation of 37, furnished the ketone 38 [Mass: m/e 236. IR (Fig. 34): OH 3520 cm^{-1}, six-membered C=O 1715 cm^{-1}, C=C 1450, 840 cm^{-1}.

+ This nomenclature is based on the name of the parent JH-I; 3" : 7", 5 : 7" indicates that these positions are joined together to form perhydroindane ring. Similar nomenclature is well-known in steroid field.



REAGENTS : 1. $NaBH_4$ / EtOH ; 2.  / Mg / Et_2O ; 3. CrO_3 / Pyridine / CH_2Cl_2 ; 4. $(EtO)_2P(O)CH_2CO_2Me$ / NaOMe / DMF ; 5. m-Cl-$PhCO_3H$ / CH_2Cl_2 ; 6. TsCl / Pyridine.

FIG. 8 : Towards the synthesis of cis-perhydroindane analogue of JH-I ; 6

PMR (Fig. 35): $\underline{Me}_2$ C=C, 6H, two ss, 1.61 ppm, 1.66 ppm; C$\underline{H}$=C, 1H, t, 5.06 ppm, J = 8Hz]. Modified Wittig reaction of the ketone 38 with methyldiethylphosphonoacetate in presence of NaOMe/DMF[19] yielded a mixture of two geometrical isomers (Z and E) of 39 [Mass: m/e 292. IR (Fig. 36): OH 3540 cm^{-1}, C=O 1744 cm^{-1}, C=C 1652, 1448, 845 cm^{-1}. PMR (Fig. 37): $\underline{Me}_2$ C=C, 6H, two bs, 1.61 ppm, 1.66 ppm; COO$\underline{Me}$, 3H, d, 3.62 ppm, J=2Hz; C$\underline{H}$=C, 1H, t, 5.06 ppm, J=8Hz; C=C$\underline{H}$COOMe, 1H, bs, 5.50 ppm, W_H=12 Hz]. Epoxidation[22] of 39 with m-Cl-$PhCO_3H$ in CH_2Cl_2 afforded, in excellent yield the required epoxide 40 in the racemic form [Mass: m/e 308. IR (Fig. 38): OH 3560 cm^{-1}, C=O 1740 cm^{-1}, C=C 1642, 860 cm^{-1}. PMR (Fig. 39): $\underline{Me}_2$ C$\underset{O}{\diagup\!\diagdown}$C, 6H, two ss, 1.02 ppm, 1.12 ppm; COO$\underline{Me}$, 3H, ss, 3.62 ppm; C=C$\underline{H}$COOMe, 1H, bs, 5.46 ppm, W_H=14Hz]. In an attempt of converting 40 to targeted JH-mimic 6 with TsCl/pyridine, starting epoxide 40 was recovered.

EXPERIMENTAL

For general remarks, see Section-I.

4-Methyl-3-pentenyl bromide; 36

To a mechanically stirred soln of NaOH (18 g) in H_2O (18 ml), was added 5-Cl-2-pentanone (36.1 g) during 15 min, and heated to boiling for 1 hr. To this was then added H_2O (37 ml) slowly (20 min), and refluxed (1 hr). Then the condenser was arranged for distillation, and a H_2O-ketone mixture was distilled off, from the reaction mixture. The aq layer was saturated (solid K_2CO_3), extracted with Et_2O (20 ml x 4), dried ($CaCl_2$), and fractionated: colorless liquid of acetyl-cyclopropane (19.2 g, 77%); b.p. 110-112° (lit.[66] b.p. 110-112°).

This acetyl cyclopropane (27 g) in dry Et_2O (100 ml) was added at room temp, to a mechanically stirred soln of Grignard reagent prepared from Mg (12.3 g), and CH_3I (72 g) in dry Et_2O (200 ml), under dry N_2. After stirring for 6 hrs at room temp, it was decomposed with sat. NH_4Cl soln, extracted with Et_2O (75 ml x 4), washed, dried, and evaporated: colorless liquid of methyl cyclooropyl carbinol (27 g, 84%); b.p. 120-121° (lit.[29] b.p. 121-122°).

This carbinol (20 g) was added (2 min) to an ice-cold,

and vigorously stirred soln of HBr (60 ml, 48%) at 10-15°, and further stirred (10 min). It was then extracted with light petroleum (75 ml x 3), washed, dried, and evaporated: colorless liquid of 36 (24 g, 74%); b.p. 62-64°/25 mm (lit.[29] b.p. 60°/25 mm).

1:7", 5:7"-cis-Cyclo-11-methyl-7-ethyl-10-dedecene-3,7-diol; 37

A soln of hydroxy ketone 26 (2.5 g) in dry ether (5 ml) was added to a stirred and ice-cooled soln of Grignard reagent prepared from the bromide 36 (8.15 g), and Mg (1.2 g) in ether (50 ml), under N_2. After stirring (10 hrs.) at room temp, the reaction mixture was decomposed with sat. NH_4Cl soln, extracted with Et_2O (50 ml x 3), washed, dried, and evaporated: olefinic diol of 46 (2.3 g, 57%).

1:7",5:7"-cis-Cyclo-7-hydroxy-11-methyl-7-ethyl-10-dodecene-3-one; 38

To a stirred soln of olefinic diol 37 (2 g) in acetone (25 ml) was added Jone's reagent (2.5 ml) at 5 to 7°, till the color of the reagent persisted (4 hrs). Then H_2O (15 ml) was added to the reaction mixture, acetone evaporated, residue diluted with H_2O (15 ml), neutralized (solid $NaHCO_3$), extracted

with Et_2O (30 ml x 3), washed, dried, and evaporated: yellowish oil (1.4 g) which was chromatographed on a silica gel column (25 cm x 1.5 cm) with C_6H_6 to EtOAc to furnish pure desired ketone 38 (1.1 g, 55%); b.p. 152-156°(bath)/0.1 mm. n_D^{26} 1.5000. R_f 0.66 (Tlc: 50% EtOAc in C_6H_6) (95% purity by glc, 5% carbowax 20M, 6', 190°, 60 ml/min, R_t 6.5 min). IR (Fig. 34): ($CHCl_3$): OH 3520 cm^{-1}, 2955 cm^{-1}, six-membered C=O 1715 cm^{-1}, C=C 1450 cm^{-1}, 1390, 1240, 1120, 1060, 960, 920 cm^{-1}, C=C 840 cm^{-1}. PMR (Fig. 35): $\underline{Me}_2$.C=C, 6H, two ss, 1.61 ppm, 1.66 ppm; CH, CH_2, 16H, m, 1.2-2.7 ppm; $\underline{OH}$, 1H, bs, 2.25 ppm; $\underline{CH}$=C, 1H, t, 5.06 ppm, J=8Hz. Mass: m/e 236 (M^+, 3.3%), 218 (100%), 160 (46.2%), 151 (35.2%), 147 (22%), 135 (30.8%), 95 (52.7%), 92 (28.6%), 83 (41.8%), 82 (69.2%), 69 (74.7%), 55 (34.1%). (Found: C, 76.2; H, 10.4. $C_{15}H_{24}O_2$ requires: C, 76.27; H, 10.17%).

Methyl 3:7",5:7"-cis-cyclo-7-hydroxy-11-methyl-3,7-diethyl-2,10-dodecadenoate; 39

$(EtO)_2P(O)CH_2COOMe$ (1.26 g) was added to a stirred suspension of NaOMe (0.65 g) in DMF (10 ml), and stirred (30 min) at room temp, under N_2. To this clear soln of phosphonate carbanion, was added a soln of ketone 38 (0.7 g) in DMF (2 ml), stirred (6 hrs) at room temp, and left overnight. This was then diluted with H_2O (50 ml), extracted with ether (20 ml x 4), washed, dried, and evaporated: colorless oil of

39 (0.59 g, 67.3%); b.p. 165-167°(bath)/0.05 mm. n_D^{26} 1.5020. R_f 0.72 (Tlc: 50% EtOAc in C_6H_6). [98% purity by glc, 5% carbowax 20M, 6', 210°, 60ml/min, two geometrical isomers with R_t 8.75 min (66%), 10.5 min (34%)]. IR (Fig. 36): ($CHCl_3$): OH 3540 cm^{-1}, 3010, 2950 cm^{-1}, C=O 1744 cm^{-1}, C=C 1652, 1448 cm^{-1}, 1390, 1270, 1170, 1130, 1040, 985, 902 cm^{-1}, C=C 845 cm^{-1}. PMR (Fig. 37): $\underline{Me}_2C=C$, 6H, two bs, 1.61 ppm, 1.66 ppm; $O\underline{H}$, 1H, bs, 2.9 ppm; $COO\underline{Me}$, 3H, d, 3.62 ppm, J=2Hz; $C\underline{H}=C$, 1H, t, 5.06 ppm, J=8Hz; $C=C\underline{H}.COOMe$, 1H, bs, 5.50 ppm, W_H=12Hz; CH, CH_2, 16H, m, 1.2-2.6 ppm. Mass: m/e 292 (M^+, 3.8%), 274 (100%), 145 (20%), 131 (25%), 119 (15%), 109 (16.3%), 107 (16.3%), 91 (43.8%), 82 (22.5%), 81 (20%), 69 (46.3%). (Found: C, 74.1; H, 9.4. $C_{18}H_{28}O_3$ requires: C, 73.9; H, 9.59%).

dl-Methyl 3":7",5:7"-cis-cyclo-10,11-epoxy-7-hydroxy-11-methyl-3,7-diethyl-2-dodecenoate; 40

A soln of m-Cl-$PhCO_3H$ (131.7 mg, 65.5%) in CH_2Cl_2 (6 ml) was added to a stirred soln of the dienoic ester 39 (146 mg) in CH_2Cl_2 (5 ml) at 0° during 10 min. After stirring (4 hrs) at 5-10°, the reaction mixture was diluted with CH_2Cl_2, washed with 5% $NaHCO_3$ aq (5 ml x 1), H_2O (5 ml x 2), washed, dried, and evaporated: colorless oil of 40 (130 mg, 85.5%). R_f 0.5 (Tlc: 50% EtOAc in C_6H_6). IR (Fig. 38): (CCl_4): OH 3560 cm^{-1}, 2930 cm^{-1}, C=O 1740 cm^{-1}, C=C 1642 cm^{-1}, 1430, 1370, 1330, 1242,

1218, 1148, 1048, 1015, 945 cm^{-1}, C=C 860 cm^{-1}. PMR (Fig. 39): $\underline{Me}_2$-C(—O—)—C, 6H, two ss, 1.02 ppm, 1.12 ppm; O$\underline{H}$, 1H, bs, 2.9 ppm; COO$\underline{Me}$, 3H, ss, 3.62 ppm; C=C$\underline{H}$.COOMe, 1H, bs, 5.46 ppm, W_H=14Hz; C$\underline{H}$, C$\underline{H}_2$, 17H, m, 1.2-2.6 ppm. Mass (Fig. 39A): m/e 308 (M^+, 3.3%), 290 (13%), 250 (60.9%), 217 (50%), 207 (55.4%), 204 (34.8%), 145 (32.6%), 131 (37%), 93 (41.3%), 79 (37%), 59 (76.1%). (Found: C, 70.2; H, 9.4. $C_{18}H_{28}O_4$ requires: C, 70.13; H, 9.09%).

dl-Methyl 3":7",5:7"-<u>cis</u>-cyclo-10,11-epoxy-11-methyl-3,7-diethyl-2,7-dodecadienoate; <u>6</u>

A soln of epoxy alcohol <u>40</u> (76 mg), Tosyl chloride (110 mg), and pyridine (5 ml) was refluxed (3 hrs). This was then diluted with H_2O (15 ml), extracted with ether (5 ml x 4), washed, dried, and evaporated to give starting epoxy alcohol <u>40</u>.

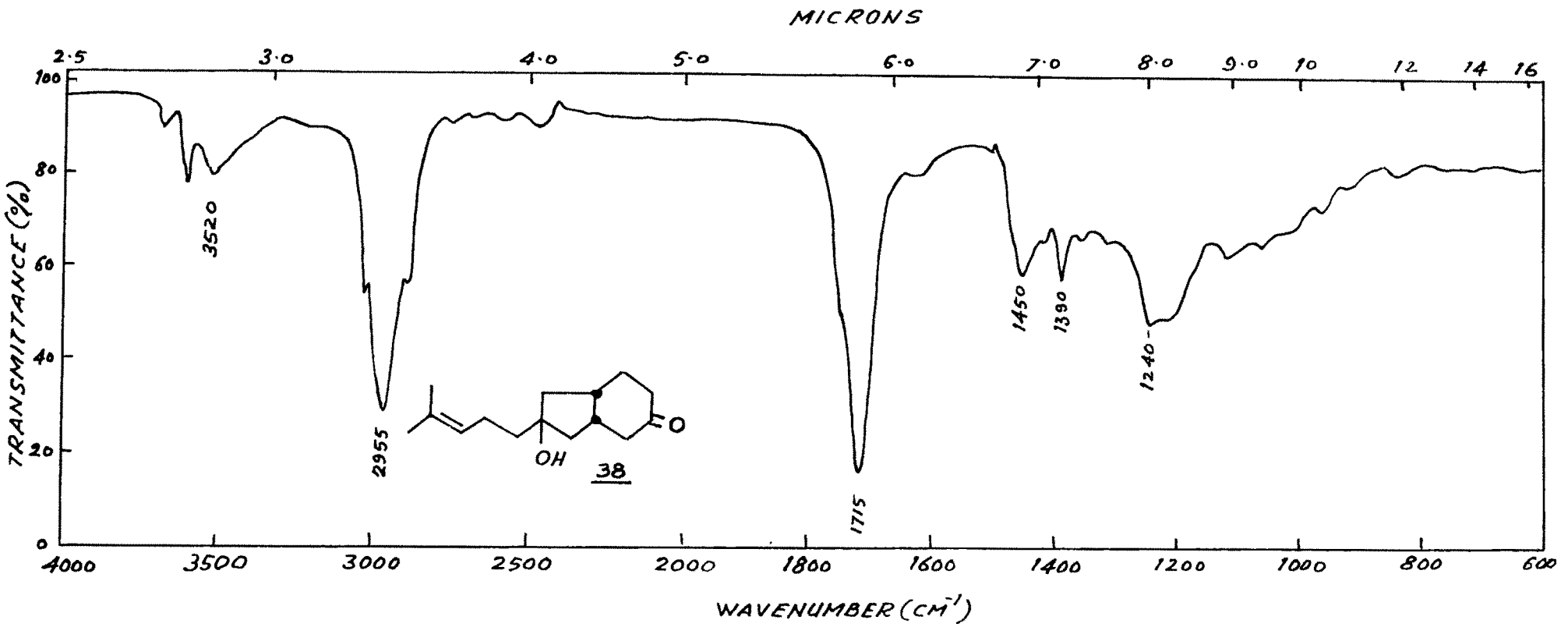


FIG. 34-IR SPECTRUM OF 1:7", 5:7"-CIS-CYCLO-7-HYDROXY-11-METHYL-7-ETHYL-10-DODECENE-3-ONE, 38

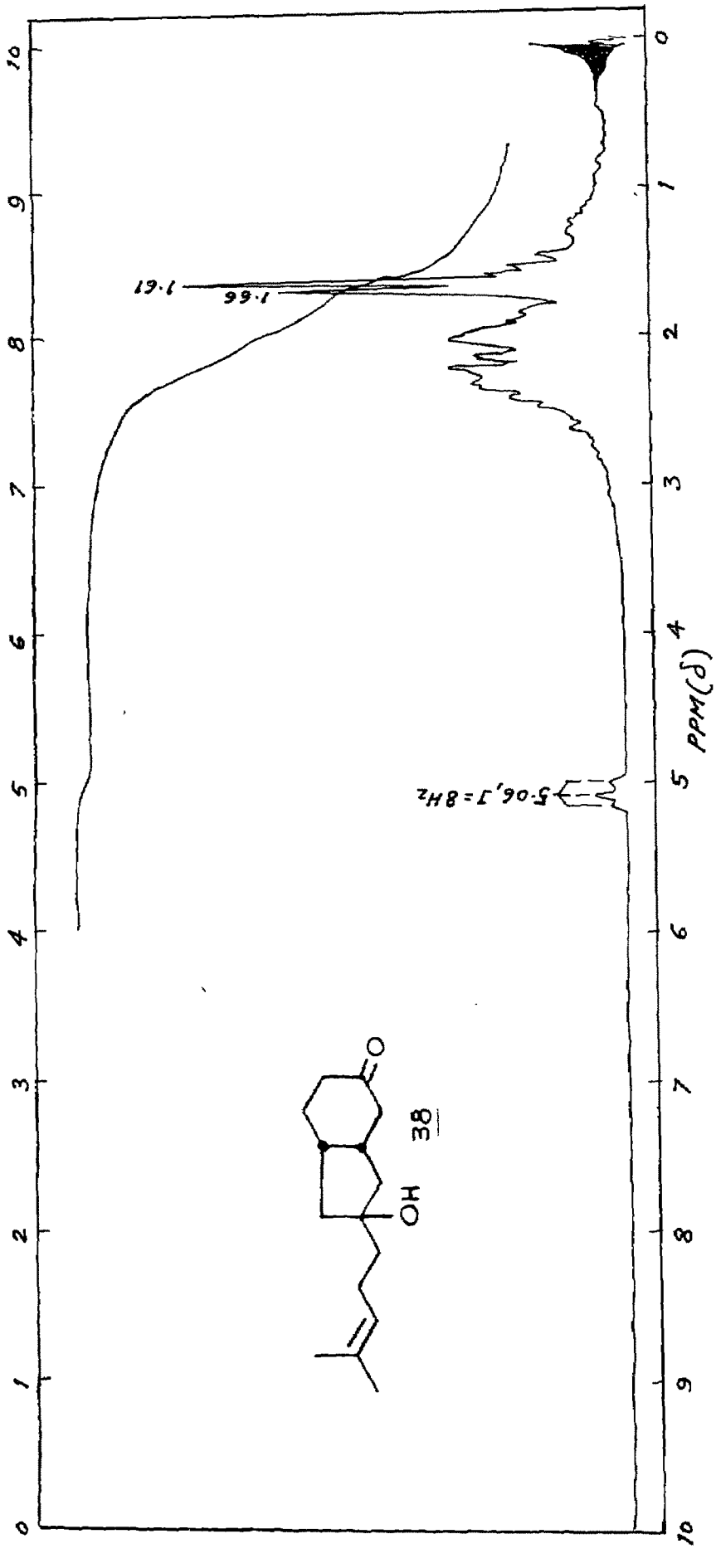


FIG. 35- NMR SPECTRUM OF 1:7, 5:7"-CIS-CYCLO-7-HYDROXY-11-METHYL-7-ETHYL-10-DODECENE-3-ONE, 38

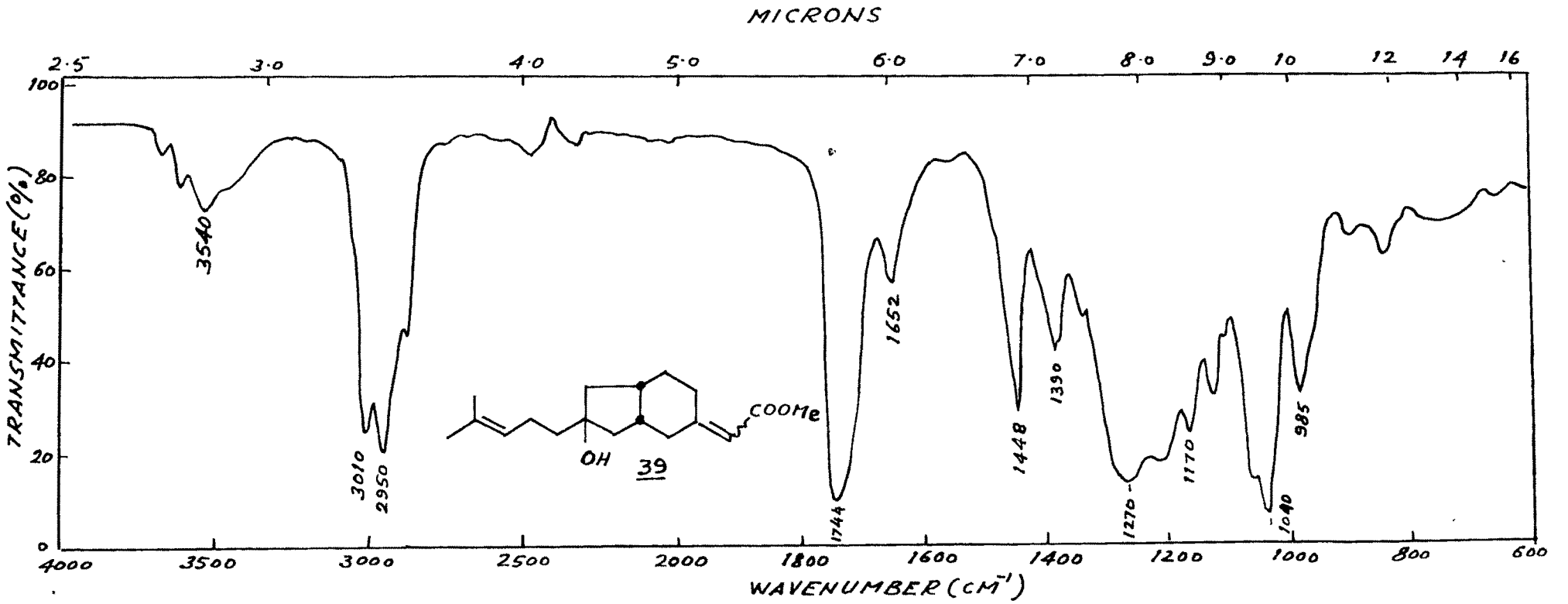


FIG. 36 - IR SPECTRUM OF METHYL 3",7",5:7"-CIS-CYCLO-7-HYDROXY-11-METHYL-3,7-DIETHYL-2,10-DODECADIENOATE, 39

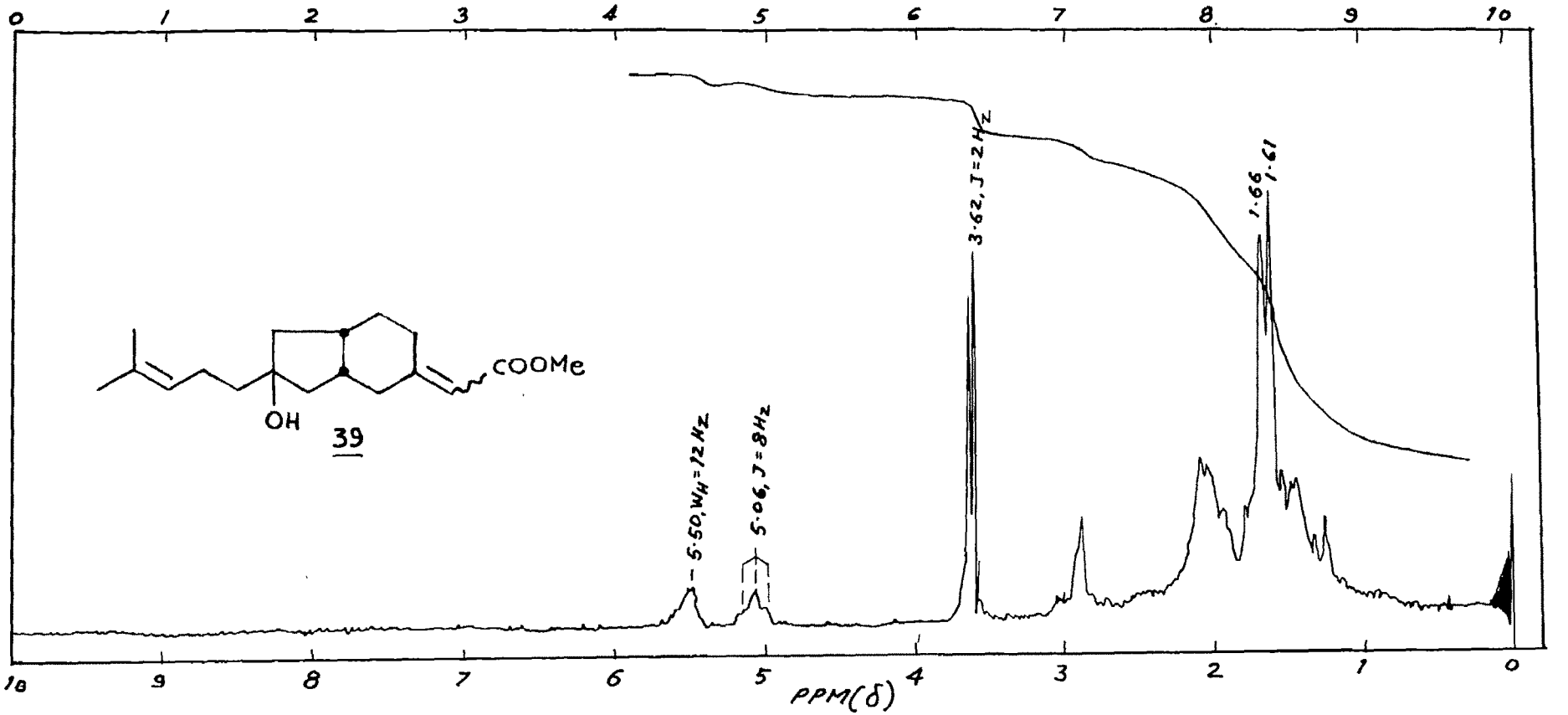


FIG.37- NMR SPECTRUM OF METHYL 3":7",5:7"- CIS- CYCLO-7 - HYDROXY - 11- METHYL-3,7 - DIETHYL - 2,10 - DODECADIENOATE ; 39

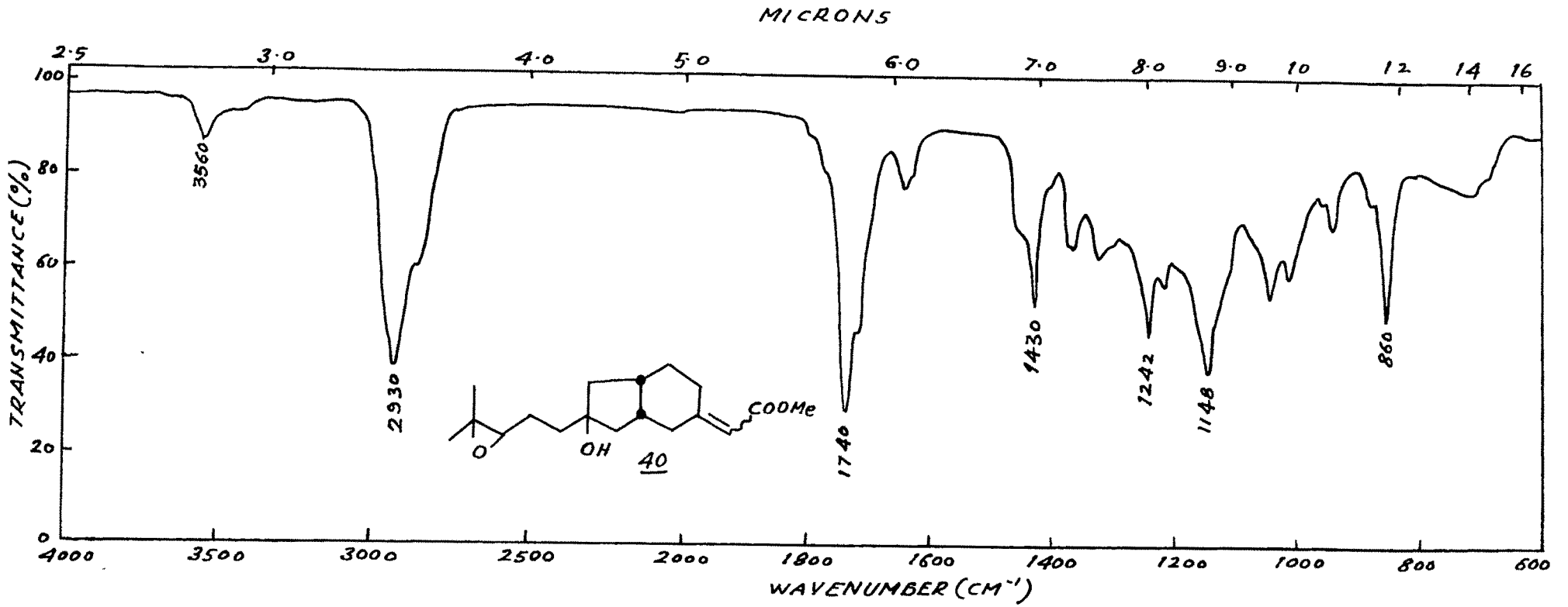


FIG. 38 - IR SPECTRUM OF DL - METHYL 3":7",5:7"- CIS - CYCLO - 10-11- EPOXY - 7 - HYDROXY - 11 - METHYL - 3,7 - DIETHYL - 2 - DODECENOATE; 40

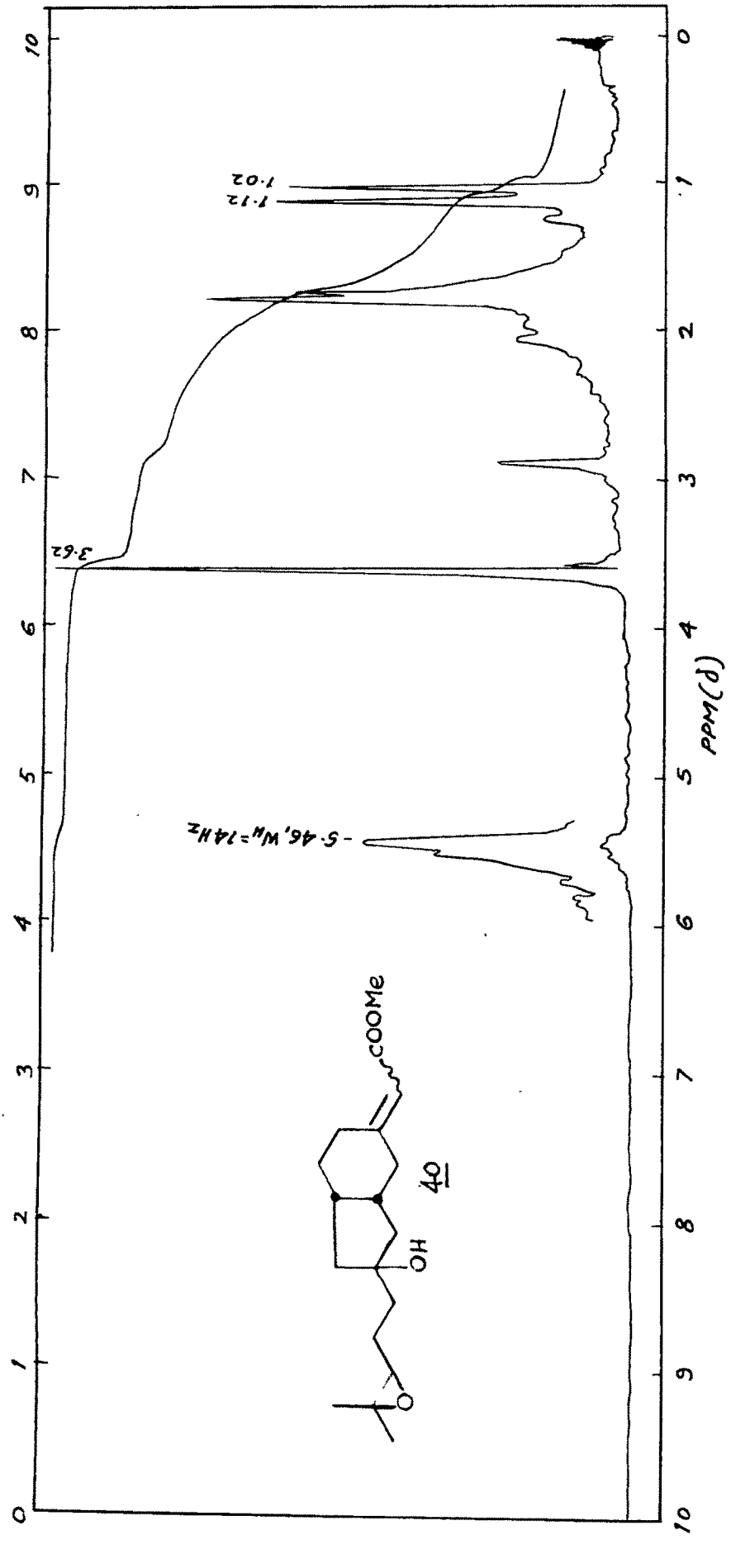


FIG.39- NMR SPECTRUM OF DL - METHYL 3:7",5:7"- CIS- CYCLO - 10,11- EPOXY-7-HYDROXY-11-METHYL-3,7-DIETHYL-2-DODECENOATE, 40

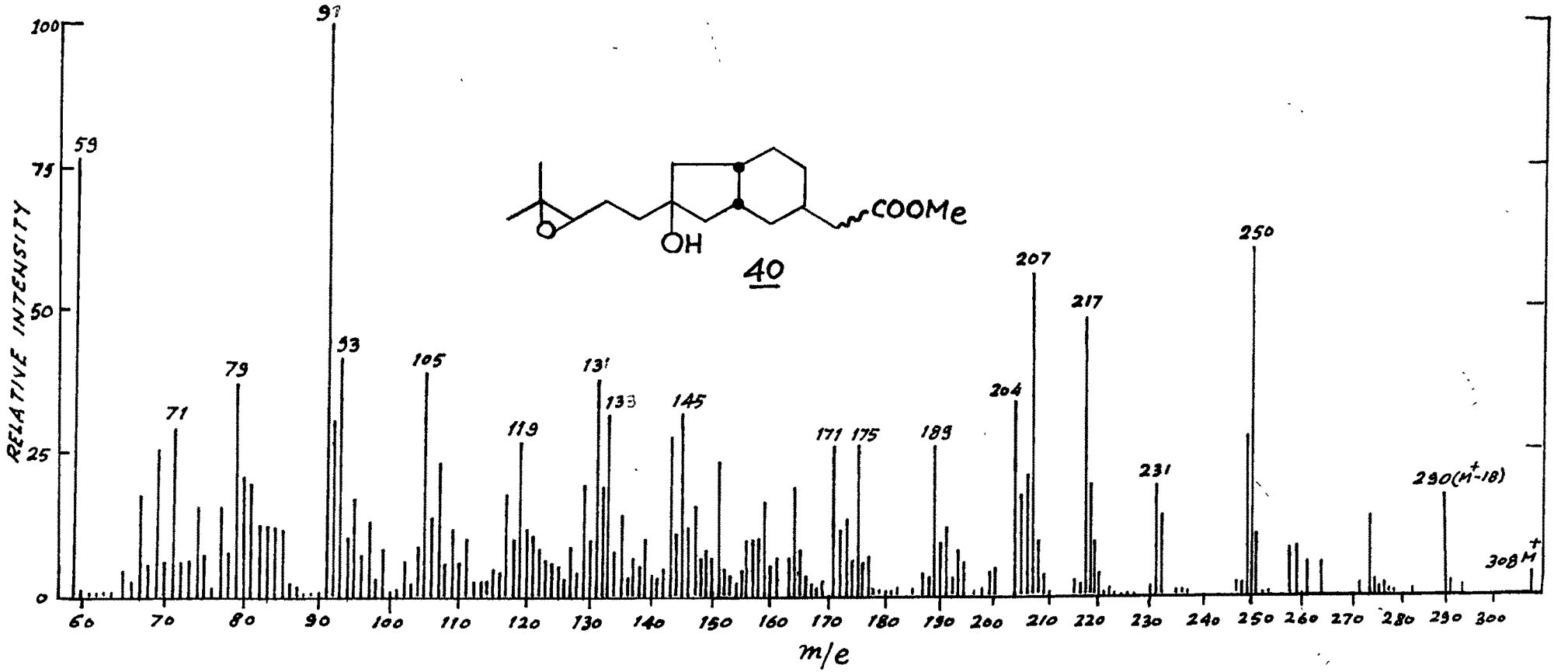


FIG. 39 A - MASS SPECTRUM OF DL-METHYL 3":7", 5:7" - CIS - CYCLO-10,11-EPOXY-7-HYDROXY-11-METHYL-3,7-DIETHYL-2-DODECENOATE; 40

SECTION–III

CYCLONONANE ANALOGUE OF CECROPIA JUVENILE HORMONE

dl - Methyl 7" : 13 - cyclo - cis - 10, 11 - epoxy - 7 - ethyl - 3, 11 - dimethyl - trans - 2, ε - 6 - tridecadienoate.

CYCLONONANE ANALOGUE OF *CECROPIA* JUVENILE HORMONE

INTRODUCTION

This section describes the efforts directed for the synthesis of dl-methyl 7" : 13-cyclo-*cis*-10,11-epoxy-7-ethyl-3,11-dimethyl-*trans*-2, ξ -6-tridecadienoate;[+] 7. 7 has been derived from JH-I ring closures at positions 7":13 (Fig. 2) and has 2 hydrogens less and decreased conformational flexibility than JH-I.

RESULTS AND DISCUSSION

5-Methyl-cyclonon-4(Z)-en-1-one; 42

For the synthesis of 7, 5-methyl-cyclonon-4(Z)-en-1-one; (42) appeared to be a logical and convenient starting point. The preparation of 42 has, apparently, not been described so far. Suitably constituted 1,3-glycols can be made to fragment generating olefinic ketones, in which the ethylenic linkage is formed in a stereospecific manner.[32] This reaction (Fig. 9) appeared most suitable for the synthesis of 42.

ξ Either Z or E geometry.

[+] This nomenclature is based on the name of parent *Cecropia* juvenile hormone (1); 7":13 indicates that these positions are joined together to form cyclononane ring. Similar nomanclature is well-known in steroid field.

The required diol 52 was prepared from the known 2-methyl cyclopentane-1,3-dione,[33] along the lines indicated in Fig. 10. The diketone 43 was transformed to the triketone 44 with methyl vinyl ketone/H_2O.[34] Aldol condensation of 44 with p-toluene sulfonic acid in benzene furnished the required bicyclic dione 45.[35,36] Sodium borohydride-ethanol[35,36] reduction of 45 yielded, in high yield the known bicyclic keto alcohol 46. The ketol 46 was converted to the olefinic alcohol 48 via the thioketal 47 either by desulfurization with Raney Ni, W_2[37] or with sodium-liquid ammonia.[38] The olefin 48 on exposure to perbenzoic acid in dichloromethane, furnished the desired epoxy derivative, in which the oxirane function is considered to be β-oriented (49), in view of the known[39] assistance from a hydroxyl function in directing the per acid attack in a non-polar solvent. Refluxing of 49 with LAH in THF yielded, in excellent yield, a crystalline diol, which from it's PMR spectrum was clearly the required 50, as anticipated.[40] Pyridine-chromic acid[41] oxidation of 50 furnished ketol 51. Hydride reduction of 51 was expected to occur from the convex face of the molecule, possibly further assisted[42] by the 1β-hydroxyl, to give essentially 52. In practice, $NaBH_4$-MeOH reduction of 51 afforded a single crystalline diol, which was distinct from 50 (m.p. IR, PMR)[43] and is thus clearly the required 52. The secondary hydroxyl in 52 was readily esterified with p-toluene sulfonyl chloride and pyridine to give 41. This mono-tosylate (41) on treatment with NaH in THF (35°, 24 hr) smoothly

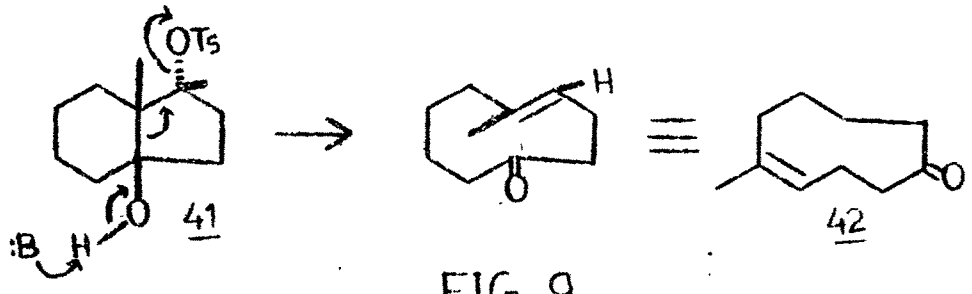
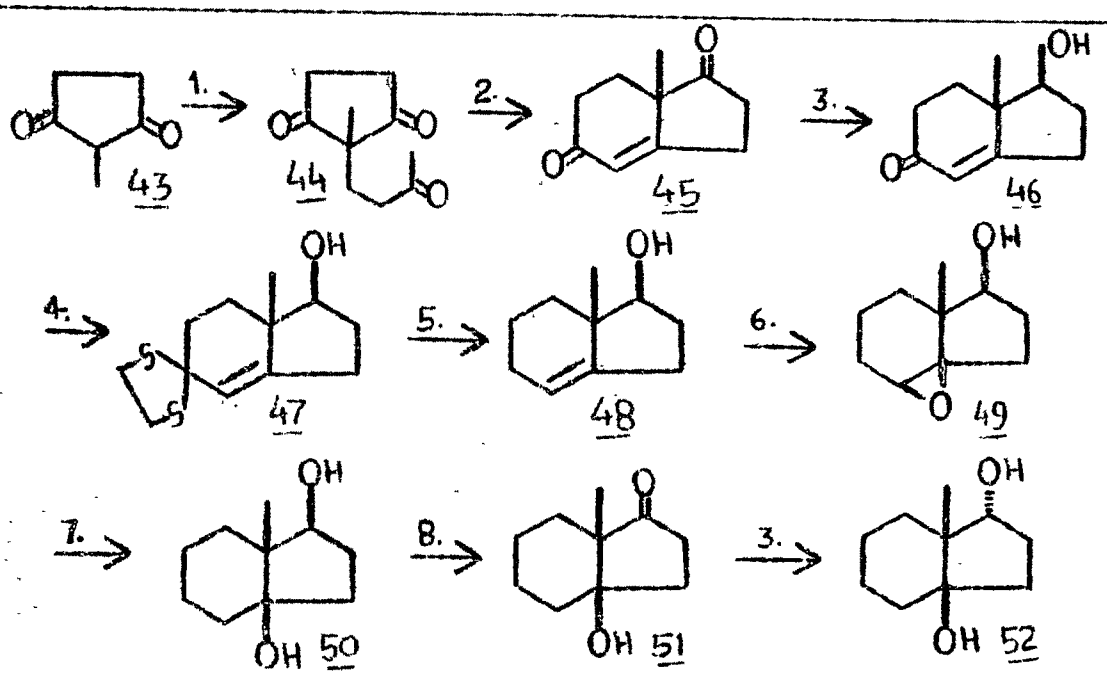


FIG. 9



REAGENTS: 1. Methyl vinyl ketone / H_2O ; 2. PTS / C_6H_6 ; 3. $NaBH_4$ / EtOH ; 4. Ethanedithiol / $BF_3{\cdot}Et_2O$ / MeOH ; 5. Liq. NH_3 / Na / Ether ; 6. Ph_3CO_3H / CH_2Cl_2 , 7. LAH / THF; 8. CrO_3 / Py., CH_2Cl_2

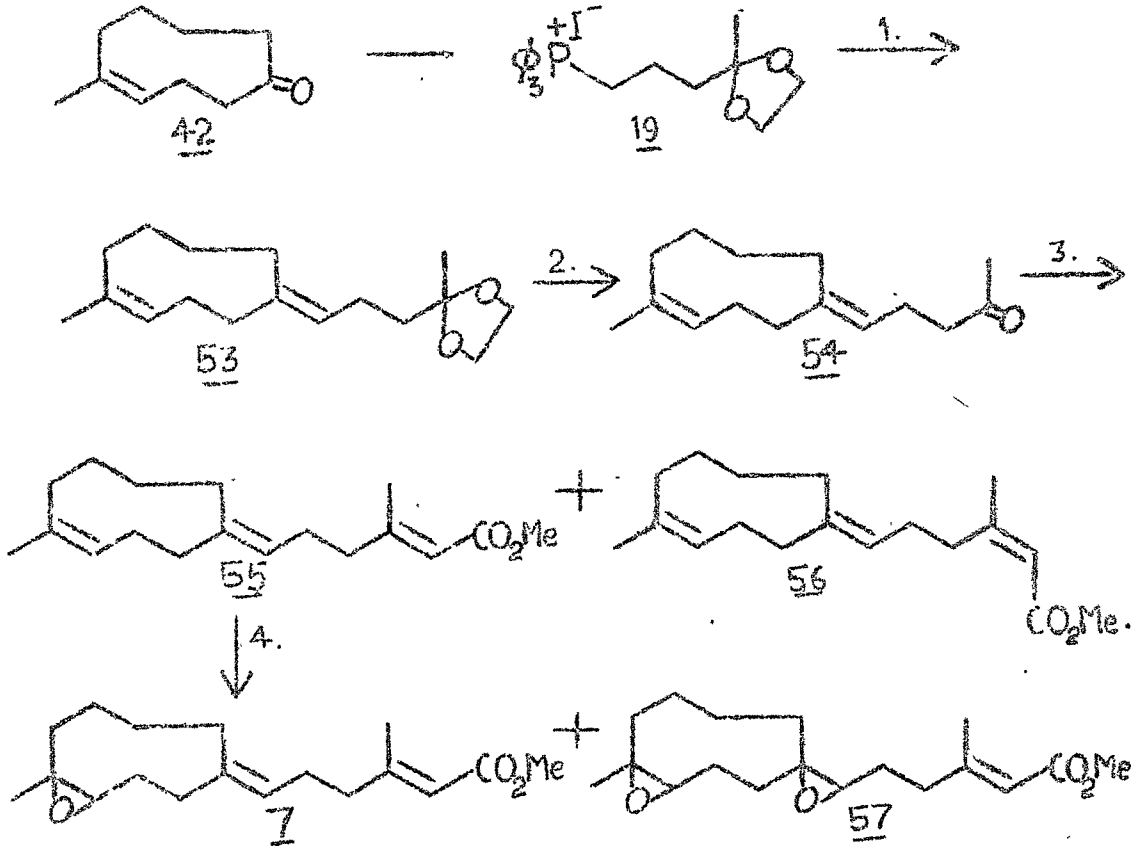
FIG. 10 Synthesis of 6β-Methyl-bicyclo(4,3,0)nonan-1β, 7α-diol

underwent the expected cleavage (Fig. 9) to furnish the anticipated 5-methyl-cyclonon-4(Z)-en-1-one [42; Mass (Fig.53A): m/e 152. IR (Fig.52): C=O 1705 cm^{-1}, C=C 1450, 860 cm^{-1}. PMR (Fig. 53): Me C=CH, 3H, 1.63 ppm, bs; Me C=CH, 1H, 5.50 ppm, bm, W_H=14Hz], the Z geometry of the olefinic linkage arising [32] from the anti-configuration of the methyl and the leaving group in 41.

Since the configuration of the tertiary hydroxyl in 41 is not relevant for fragmentation to 42, attempts were made in the initial stages of this investigation for inversion of the hydroxyl configuration in 48 by several methods[44], but without much success.

Cyclononane analogue of JH-I; 7

The reaction sequence successfully followed for the synthesis of cyclononane analogue of JH-I; 7 from 42 is briefly summarised in Fig. 11. The olefinic ketone 42 was transformed to the dienoic ketal 53 by Wittig reaction with the phosphonium salt 19,[17] in presence of potassium-t-butoxide-tetrahydrofuran. This ketal 53 was readily hydrolysed with p-toluene sulfonic acid-acetone to afford the dienoic ketone displaying spectral characteristics expected of 54 [Mass(Fig.55A): m/e 220. IR (Fig.54): C=O 1720 cm^{-1}, C=C 1445, 855 cm^{-1}. PMR (Fig.55): Me C=C, 3H, 1.60 ppm, bs; COMe, 3H, 2.04 ppm, ss; CH=C, 1H, 5.18 ppm, t, J=6Hz; Me C=CH, 1H, 5.46 ppm, bm, W_H=15Hz. Glc: R_f 7.0 min (98%), 5% carbowax 20M, 6', 60 ml/min, 190°], the ζ (either Z or E) geometry of $\Delta^{5,6}$



REAGENTS: 1. K-t-butoxide / THF ; 2. PTS / Acetone ;
3. $(MeO)_2P(O)CH_2CO_2Me$ / NaOMe / DMF ; 4. m-Cl-$PhCO_3H$ / CH_2Cl_2

FIG. 11 Synthesis of cyclononane analogue of JH-I ; 7

double bond remains unsolved, because it is not possible to deduce steriochemistry from the PMR data or from analysis of similar cases.[17] Condensation of the ketone 54 with trimethyl-phosphono acetate[28] in presence of sodium methoxide-dimethyl-formamide[19] gave rise to a mixture of E and Z isomers (55 and 56) of the trienoic ester, could readily be separated by inverted-dry-column-chromatography (IDCC)[20], and identified, as one would expect different chemical shift in PMR (Fig. 57 and 59) for C_3-methyl signal for the E-(55, 2.13 ppm), and Z-isomers (56, 1.88 ppm).[21] The E-ester was epoxidized[22] with m-Cl-perbenzoic acid[23] in dichloromethane at 0^{o}. Tlc separation of the resulting epoxides (7 and 57) afforded the targeted cyclononane analogue of Cecropia juvenile hormone in racemic form [7; Mass (Fig. 61A): m/e 292. IR (Fig. 60): C=O 1720 cm^{-1}, C=C 1645, 1432 cm^{-1}. PMR (Fig. 61): Me C—C (O); 3H, 1.20 ppm, ss; Z-Me C=C COOMe, 3H, 2.13 ppm, ss; COOMe, 3H, 3.62 ppm, ss; CH=C, 1H, 5.12 ppm, m, W_H=12Hz; C=CH COOMe, 1H, 5.58 ppm, bs].

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

For general remarks, see Section-I.

2-Methyl-cyclopentane-1,3-dione; 43

Propionyl chloride was prepared by following the procedure of H.C. Brown et al.[47]

To a stirred soln of $MeNO_2$ (200 ml), and anhydrous $AlCl_3$ (200 g) was added succinic acid (59 g) in portions during 1 hr at room temp, and further stirred (3.5 hrs) till the evolution of HCl gas had subsided. To this thick brownish slurry was added CH_3CH_2COCl (139 g) during 30 min at room temp, and stirred (3 hrs) at 80°. The reddish reaction mixture was then poured onto ice-pieces (400 g), and left overnight at -10°, the precipitated product was filtered, washed with 10% NaCl aq, toluene, dried, taken in hot H_2O (1500 ml), treated with charcoal (6.5 g) at 90° (20 min), filtered, concentrated (300 ml), and cooled (0°), whereupon white crystals of 43 precipitated which was filtered and dried (38g, 72%); m.p. 212-214° (lit.[33] 212-214°).

2-Methyl-2-(3-oxobutyl)-cyclopentane-1,3-dione; 44

To a suspension of the diketone 43 (32.5 g) in demineralized H_2O (68 ml) was added at once freshly distilled methyl vinyl

ketone (48 ml) and stirred (5 days) at 25°, under N_2. It was then extracted with C_6H_6 (50 ml x 6), dried, and evaporated to afford the crude triketone 44 (49.5 g, 94.6%) which on fractionation furnished pure triketone 44 (45 g, 86%); b.p. 90-95°/0.05 mm (lit.[34] b.p. 100-109°/0.8-0.1 mm).

6-Methyl-bicyclo(4,3,0)non-1-en-3,7-dione; 45

A soln of triketone 44 (45 g) in C_6H_6 (250 ml) was refluxed with p-toluene sulfonic acid (2 g) in a Dean-Stark unit for 2 hrs. After that again p-toluene-sulfonic acid (2 g) was added and further refluxed (5 hrs). The reddish soln was then filtered, neutralized (solid K_2CO_3), filtered, washed, dried, and evaporated: pale-yellow oil (32 g, 79.3%), b.p. 100-108°/0.1 mm which on cristallization from ether: light petroleum (2:1) furnished large cristals of 45 (30 g, 74.3%), m.p. 71-72° (lit.[35] m.p. 72-73°).

6β-Methyl-bicyclo(4,3,0)non-1-en-7β-01-3-one; 46

To a stirred soln of bicyclic dione 45 (16.4 g) in EtOH (250 ml), was added a soln of $NaBH_4$ (1.02 g) in EtOH (100 ml) at 0-5° during 1 hr, and further stirred (2 hrs). The resulting dark greenish soln was then neutralized with HOAc (2.5 ml), EtOH evaporated, residue dissolved in $CHCl_3$ (350 ml), washed, dried and evaporated: pale yellow oil

(13 g, 82%), b.p. 139-144°/0.05 mm. (lit. b.p. 140-145°/0.05 mm). IR (CCl_4): OH 3420 cm^{-1}, 2980, 2860 cm^{-1}, C=O 1705 cm^{-1}, C=C 1662, 1462 cm^{-1}, 1420, 1365, 1320, 1268, 1220, 1135, 1090, 1078, 1008, 960, 872 cm^{-1}. PMR ($CDCl_3$): Me.C, 3H, ss, 1.15 ppm; CH_2, OH, 9H, m, 1.6-3.0 ppm; CHOH, 1H, t, 3.84 ppm, J=4.5 Hz; C=CH.CO, 1H, bs, 5.78 ppm.

3,3-Ethylenedithio-6β-methyl-bicyclo(4,3,0)non-1-en-7β-ol; 47

To a soln of the α,β-unsaturated ketone 46 (16.6 g), and ethanedithiol (14.1 g) in CH_3OH (120 ml), was added BF_3.Et_2O (14 ml) at 0-5° during 10 min, and left overnight to come at room temp. The resulting soln was then poured into ice cold 10% NaOH aq (250 ml), extracted with $CHCl_3$ (75 ml x 4), washed with H_2O (100 ml x 2), washed, dried, and evaporated: white crystalline solid of 47 (21.7 g, 90%), m.p. 105-106°. IR (Fig. 40): ($CHCl_3$): OH 3420 cm^{-1}, 2910, 2840, 1660 cm^{-1}, C=C 1450 cm^{-1}, 1440, 1425, 1370, 1330, 1270, 1210, 1060, 1025, 998, 972 898, 865 cm^{-1}, C=C 844 cm^{-1}. PMR (Fig. 41): ($CDCl_3$): Me.C, 3H, ss, 0.97 ppm; S.CH_2.CH_2.S, 4H, q, 3.33 ppm, J_1=7Hz, J_2=4Hz; CHOH, 1H, t, 3.65 ppm, J=8Hz; C=CH-S.CH_2.CH_2.S, 1H, bs, 5.47 ppm, W_H=5Hz; CH_2, OH, 9H, m, 1.3-2.5 ppm. Mass: m/e 242 (M^+, 84.6%), 214 (55.1%), 182 (54.5%), 149 (27.2%), 138 (41.7%), 131 (53.2%), 118 (67.9%), 105 (100%), 91 (37.8%), 61 (41.7%), 60(30.1%), 59 (28.8%).

6β-Methyl-bicyclo(4,3,0)non-1-en-7β-ol; 48

(i) A mixture of thioketal 47 (2 g), Raney Ni., W_2 (10 g), and EtOH (150 ml) was refluxed (20 hrs) under N_2. It was then transferred to a Soxhlet unit and continuously extracted (24 hrs). EtOH evaporated to afford yellowish solid which was filtered through a silica gel column (30 cm x 1.4 cm) with C_6H_6: EtOAc (9:1) to furnish white crystalline solid of 48 (0.82 g, 65%); b.p. 90-95°(bath)/0.05 mm; m.p. 51-52°, (96% purity by glc, 10% carbowax 20M, 6', 190°, 60 ml/min, R_t 4.9 min). IR (Fig. 42): (CCl_4): OH 3360 cm^{-1}, 2920, C=C 1455 cm^{-1}, 1430, 1370, 1335, 1315, 1295, 1260, 1120, 1055, 1020, 984, 925, 878 cm^{-1}, C=C 852 cm^{-1}. PMR (Fig. 43): Me.C, 3H, ss, 0.88 ppm; CHOH, 1H, t, 3.52 ppm, J=8Hz; CH=C, 1H, bm, 5.23 ppm, W_H=9Hz; CH_2, 10H, m, 1.4-2.5 ppm; OH, 1H, s, 1.75 ppm. Mass: m/e 152 (M^+, 72.5%), 134 (41.3%), 119 (34.8%), 109 (65.2%), 97 (47.8%), 95 (39.9%), 93 (100%), 91 (51.4%), 81 (39.9%), 79 (52.2%), 67 (34.8%).

(ii) The thioketal 47 (12 g) in dry ether (500 ml) was added to anhydrous liq. NH_3 (1500 ml). To this Na (12 g) was added in small piecies during 10 min with continuous stirring. After 15 min, the blue color of the soln was discharged by addition of EtOH. Liq. NH_3 was evaporated, residue diluted with brine (150 ml), extracted with ether (75 ml x 4), washed

dried, and evaporated: white crystalline solid (6 g, 78.9%); b.p. 90-95°(bath)/0.05 mm; m.p. 51-52° which was identical with 48 (IR, PMR, Mass).

Epimerization of 7β-hydroxyl group of 48

(i) A soln of alcohol 48 (0.5 g) in pyridine (8 ml) was cooled to 0°, TsCl (1 g) was added in portion, and left (24 hrs) at 10-15°. The reaction mixture was then diluted with cold H_2O (30 ml), extracted with ether (25 ml x 3), washed dried and evaporated at 20° to furnish oily tosylate (0.9 g, 81.8%).

To this tosylate (0.8 g) DMF (5 ml) and H_2O (0.7 ml) was added fused KOAc (0.8 g) and stirred at 70° for 12 hrs. The contents were then diluted with H_2O (25 ml), extracted with ether (15 ml x 3), washed, dried, and evaporated to give an oily product which was taken up in CH_3OH (15 ml) and H_2O (1.5 ml). KOH (0.24 g) was then added and refluxed (3 hrs) under N_2. MeOH evaporated, residue diluted with H_2O (15 ml), acidified with dil. HCl (1:1), extracted with ether (15 ml x3), washed, dried, and evaporated: white solid of 48 (0.25 g, 50%); b.p. 90-95°(bath)/0.05 mm; m.p. 51-52°. IR, PMR examination indicated it to be the starting material 48.

(ii) A mixture of Al-isopropoxide (1 g), isopropanol (5 ml), acetone (5 ml), and the alcohol 48 (100 mg) was stirred (3 days) at 45-50°. After usual work-up, the product obtained was the starting β-alcohol 48 (80 mg).

(iii) Ethylazodicarboxylate was prepared following the procedure of J.C. Kauer.[48]

To a stirred soln of β-alcohol 48 (0.38 g), Ph_3P (1.3 g), and HCOOH (0.23 g) in THF (30 ml) was added dropwise a soln of diethyl azodicarboxylate (0.87 g) in THF (5 ml) and stirred (14 hrs) at room temp. THF evaporated: syrupy product which was chromatographed over a silica gel column (8 cm x 0.5 cm), and eluted with light petroleum: C_6H_6 (60:40) to yield the starting β-alcohol 48 (0.35 g).

1,2-β-Epoxy-6β-methyl-bicyclo(4,3,0) nonan-7β-ol; 49

To a soln of olefinic alcohol 48 (6.04 g) in CH_2Cl_2 (50 ml) was added a soln of $PhCO_3H$ (6.98 g, 85%) in CH_2Cl_2 (50 ml) over a period of 30 min at 0-5°, and further stirred for 2 hrs. The contents were then diluted with H_2O (100 ml), extracted with CH_2Cl_2 (50 ml x 3), washed with 15% K_2CO_3 aq (50 ml x 3), washed, dried, and evaporated: colorless oil of 49 (5.82 g, 87.3%); R_f 0.45 (Tlc: 10% EtOAc in C_6H_6). IR (Fig. 44): (CCl_4): OH

3460 cm^{-1}, 2950, 1468, 1444, 1380, 1215, 1140, 1090, 1040, 912, 880 cm^{-1}. PMR (Fig. 45): Me.C, 3H, ss, 0.97 ppm; C—CH (epoxide), 1H, m, 3.03-3.3 ppm; CHOH, 1H, m, 3.7-4.1 ppm; CH_2, OH, 11H, m, 1.0-2.4 ppm. Mass: m/e 168 (M^+, 24.4%), 124 (100%), 111 (32.1%), 109 (38.5%), 97 (55.1%), 95 (34.6%), 93 (37.2%), 81 (39.7%), 79 (38.5%), 66 (41%), 55 (38.5%).

6β-Methyl-bicyclo(4,3,0)nonan-1β,7β-diol; 50

To a stirred slurry of LAH (1.14 g) in THF (40 ml) was added a soln of epoxy alcohol 49 (5 g) in THF (10 ml) during 15 min at room temp, and refluxed for 6 hrs. The reaction mixture was then decomposed with minimum of cold H_2O, filtered, and residue was wahsed thoroughly with ether. The combined filterate was dried and evaporated: white crystalline solid of 50 (4.59 g, 90%); m.p. 114-115°. IR (Fig. 46): ($CHCl_3$): OH 3430 cm^{-1}, 2960, 2884, 1462, 1425, 1390, 1340, 1185, 1155, 1080, 1035, 1012, 988, 858 cm^{-1}. PMR (Fig. 47): ($CDCl_3$): Me.C, 3H, ss, 1.06 ppm; CHOH, 1H, t, 3.70 ppm, J = 6Hz; OH, 1H, bs, 2.06 ppm; OH, 1H, bs, 2.9 ppm; CH_2, 12H, m, 1.16-2.4 ppm. Mass: m/e 152 (M^+-18, 100%), 137 (78.2%), 134 (51.5%), 123 (51.0%), 109 (99%), 108 (85.1%), 107 (49.5%), 105 (69.3%), 104 (42.6%), 103 (55.4%), 81 (47.5%). (Found: C, 70.8; H, 10.8. $C_{10}H_{18}O_2$ requires; C, 70.59; H, 10.59%).

6β-Methyl-bicyclo(4,3,0)nonan-1β-ol-7-one; 51

CrO_3 (18 g), was added to a magnetically stirred soln of pyridine (28.4 g) in CH_2Cl_2 (450 ml), and the deep burgandy soln was stirred (15 min) at room temp. The diol 50 (5.1 g) in CH_2Cl_2 (10 ml) was added in one portion. A tarry black deposit separated immediately. After stirring (15 min) at room temp, the soln was decanted from the residue, which was again washed with ether (100 ml x 3). The combined organic layer was washed with 10% NaOH aq (100 ml x 3), 10% HCl aq (100 ml x 1), 10% $NaHCO_3$ aq (100 ml x 1), washed, dried, and evaporated: brownish residue which was taken up in ether (200 ml), filtered, washed with 10% $NaHCO_3$ aq (50 ml x 2), washed, dried, and evaporated: white crystalline solid of 51 (3.49 g, 68.7%); b.p. 95-100°/0.05 mm; m.p. 89-90°, IR (Fig. 48): ($CHCl_3$): OH 3460 cm^{-1}, 2940, 2870 cm^{-1}, five-membered C=O 1740 cm^{-1}, 1455, 1410, 1380, 1218, 1090, 1065, 960, 885 cm^{-1}. PMR (Fig. 49): ($CDCl_3$): Me.C, 3H, ss, 1.02 ppm; CH_2, OH, 13H, m, 1.16-2.6 ppm. Mass: m/e 168 (M^+, 83%), 150 (27.7%), 121 (22.6%), 112 (46.5%), 111 (25.2%), 109 (37.7%), 108 (100%), 97 (44.7%), 95 (57.9%), 93 (39%), 67 (25.2%), 55 (31.4%). (Found: C, 71.2; H, 9.8. $C_{10}H_{16}O_2$ requires: C, 71.43; H, 9.52%).

6β-Methyl-bicyclo(4,3,0)nonan-1β,7α-diol; 52

To a stirred soln of hydroxy ketone 51 (3.36 g) in

CH_3OH (30 ml) was added $NaBH_4$ (0.756 g) in small portions (15 min), and stirred (15 hrs) at room temp. Cold aq tartaric acid soln was added with ice cooling until the white precipitate redissolved. Almost all of the CH_3OH was evaporated, the aq. soln was extracted with ether (50 ml x 4), washed dried, and evaporated: white crystalline solid of 52 (2.97 g, 87.3%); m.p. 122-123°. IR (Fig. 50): ($CHCl_3$): OH 3470 cm^{-1}, 2950, 2970, 1480, 1470, 1392, 1355, 1145, 1070, 1025, 982, 955, 900, 870 cm^{-1}. PMR (Fig. 51): ($CDCl_3$): Me.C, 3H, ss, 1.02 ppm; CHOH, 1H, t, 4.22 ppm, J=7Hz; CH, CH_2, OH, 14H, m, 1.1-2.5 ppm. Mass: m/e 152 (M^+-18, 93.8%), 137 (87.5%), 112 (56.3%), 109(100%), 108 (73.4%), 97(78.1%), 95(100%), 93 (62.5%), 85 (59.4%), 83 (56.3%), 81 (71.9%), 67 (78.1%), 55 (71.9%). (Found: C, 71; H, 10.3; $C_{10}H_{18}O_2$ requires: C, 70.59; H, 10.59%).

7α-Tosyloxy-6β-methyl-bicyclo(4,3,0)nonan-1β-ol; 41

To a soln of the diol 52 (2.6 g) in pyridine (40 ml) was added p-toluene sulfonyl chloride (3.5 g) at 0° and left overnight at 10-15°. The reaction mixture was then diluted with cold H_2O (250 ml), extracted with ether (30 ml x 3), washed with H_2O (30 ml x 1), 50% HCl aq (30 ml x 2), washed, dried, and evaporated (20-22°) to yield pale yellow oil of 41 (4.48 g, 97%). This tosylate was satisfactory for subsequent reactions.

5-Methyl-cyclononan-4(Z)-en-1-one; 42

A soln of tosylate 41 (3.24 g) in THF (5 ml) was added to a stirred suspension of freshly prepared K-t-butoxide (3.36 g) in THF (30 ml) at room temp under N_2. After stirring (20 hrs) at room temp, the resulting yellow soln was diluted with H_2O (50 ml), brine (50 ml), extracted with ether (40 ml x3), washed, dried, and evaporated: yellow oil which was filtered through a silica gel column (15 cm x 1 cm) with light petroleum: C_6H_6, 1:1 to give colorless liquid of 42 (1.17 g, 77.4%); b.p. 115-120°(bath)/4 mm; n_D^{26} 1.4869. R_f 0.37 (Tlc: 30% light petroleum in C_6H_6). (96% purity by glc, 10% carbowax 20M, 6', 170°, 60 ml/min, R_t 10.75 min). IR (Fig. 52): (CCl_4): 2936, 2880 cm^{-1}, C=O 1705 cm^{-1}, 1470 cm^{-1}, C=C 1450 cm^{-1}, 1434, 1375, 1335, 1248, 1235, 1164, 1148, 1115, 1042, 1020, 980 cm^{-1}, C=C 860 cm^{-1}, 830 cm^{-1}. PMR (Fig. 53): Me.C=CH, 3H, bs, 1.63 ppm; Me.C=CH, 1H, bm, 5.50 ppm, W_H=14Hz; CH_2, 12H, m, 1.5-2.7 ppm. Mass (Fig. 53A): m/e 152 (M^+, 32.9%), 150 (34.3%), 108 (41.4%), 95 (47.1%), 93 (100%), 91 (42.9%), 81 (48.6%), 80 (51.4%), 79 (78.6%), 77 (45.7%), 66 (75.7%), 55 (71.4%), 53 (51.4%). (Found: C, 79.2; H, 10.6. $C_{10}H_{16}O$ requires: C, 78.95; H, 10.53%).

6":12-Cyclo-10-methyl-6-ethyl-ξ-5,cis-9-dodecadiene-2-one; 54

To a stirred suspension of freshly prepared K-t-butoxide

(1.85 g) in THF (30 ml) was added (4,4-ethylene dioxy) pentyl triphenylphosphonium iodide (19, 7.7 g), and stirred (30 min) at room temp under N_2. To this orange-phosphorane was added a soln of olefinic ketone 42 (1.52 g) in THF (3 ml) and stirred (2 hrs) at room temp. After stirring (12 hrs) at 50°, THF was evaporated, residue diluted with light petroleum (100 ml), filtered, washed, dried, concentrated (50 ml), chilled at -10 to -15° (3 hrs), filtered, and evaporated: yellowish oil of 53 which was mixed with acetone (20 ml), H_2O (5 ml), p-toluene sulfonic acid (0.1 g), and stirred (12 hrs) at room temo. Acetone evaporated, residue diluted with H_2O (25 ml), neutralized (solid K_2CO_3), extracted with light petroleum (30 ml x 4), washed, dried, and evaporated: yellow oil which was placed on a silica gel column (20 cm x 2 cm), and eluted with light petroleum: C_6H_6 (1:1) to furnish colorless liquid of 54 (1.46 g, 73%); b.p. 125-130°(bath)/0.01 mm. n_D^{26} 1.4983. R_f 0.43 (Tlc: 30% light petroleum in C_6H_6). (98% purity by glc, 5% carbowax 20M, 6', 190°, 60 ml/min, R_t 2.25 min; 98% purity by glc, 10% SE-30, 6', 190°, 60 ml/min, R_t 7.0 min; 98% purity by glc, 3% carbowax 20M, 6', 190°, 60 ml/min, R_t 2.37 min). IR (Fig. 54): (CCl_4): 2916, 2850 cm^{-1}, C=O 1720 cm^{-1}, C=C 1445 cm^{-1}, 1352, 1268, 1220, 1155, 1022, 945 cm^{-1}, C=C 855 cm^{-1}. PMR (Fig. 55): Me.C=CH, 3H, bs, 1.60 ppm; COMe, 3H, ss, 2.04 ppm; CH=C, 1H, t, 5.18 ppm, J=6Hz; Me.C=CH, 1H, bm; 5.46 ppm, W_H= 15Hz. Mass (Fig. 55A):

m/e 220 (M^+, 27.4%), 162 (66.4%), 146 (42.5%), 135 (53.1%), 107 (32.7%), 95 (42.9%), 94 (72.6%), 93 (40.7%), 81 (40.7%), 79 (100%), 66 (44.2%), 55 (40.7%). (Found: C, 82; H, 11.2. $C_{15}H_{24}O$ requires C, 81.82; H, 10.91%).

Methyl,trans,ξ,cis-and cis,ξ,cis-7":13-cyclo-7-ethyl-3,11-dimethyl-2,6,10-tridecatrienoate; 55 and 56

To a stirred suspension of NaOMe (0.552 g) in DMF (15 ml) was added $(MeO)_2P(O)CH_2COOMe$ (1.87 g) at 25°, and stirred (30 min) under N_2. To this clear soln of phosphonate carbanion was added a soln of ketone 54 (1.1 g) in DMF (2 ml) at 20°, and stirred (24 hrs) at room temp. The resulting yellow soln was then decomposed with H_2O (35 ml), extracted with Et_2O (25 ml x 4), washed, dried, and evaporated: pale yellow oil of 55 and 56 (0.98 g, 72%); b.p. 155-160°/0.01 mm. R_f 0.63, 0.66 (Tlc: 30% light petroleum in C_6H_6). [96% purity by glc, 5% carbowax 20M, 6', 220°, 60 ml/min, R_t 8.5 min (56, 34%), 11.5 min (55, 66%)].

These isomers (750 mg) were separated by inverted-dry-column-chromatography (IDCC) in the same manner as described for the separation of 22 and 23. The E-isomer 55 (340 mg) displayed the following physical properties: b.p. 155-160°/0.01 mm. n_D^{26} 1.5081. R_f 0.63 (Tlc: 30% light petroleum in C_6H_6). (95% purity by glc, 5% carbowax 20M,

6', 220°, 60 ml/min, R_t 11.5 min). IR (Fig. 56): (CCl_4): 2918, 2864 cm^{-1}, C=O 1726 cm^{-1}, C=C 1652, 1440 cm^{-1}, 1382, 1366, 1230, 1158, 1164, 930, 870 cm^{-1}. PMR (Fig. 57): Me.C=C, 3H, bs, 1.60 ppm; Z-Me.C=C.COOMe, 3H, ss, 2.13 ppm; COOMe, 3H, ss, 3.62 ppm; CH=C, 1H, bm, 5.12 ppm, W_H=12Hz; Me.C=CH, 1H, bm, 5.48 ppm, W_H=14Hz; C=CH.COOMe, 1H, bs, 5.58 ppm; CH_2, 16H, m, 1.2-3.0 ppm). Mass: m/e 276 (M^+, 14.5%), 163 (41.8%), 135 (47.2%), 114 (51.8%), 107 (60%), 103 (54.5%), 101 (52.7%), 95 (67.3%), 82 (63.6%), 81 (94.5%), 79 (90.9%), 67 (80%), 55 (100%), 53 (56.4%). (Found: C, 78.4; H, 10.2. $C_{18}H_{28}O_2$ requires: C, 78.26; H, 10.15%).

The Z-ester 56 (160 mg) showed the following physical properties: b.p. 155-160°/0.01 mm. n_D^{26} 1.5067. R_f 0.66 (Tlc: 30% light petroleum in C_6H_6). (94% purity by glc, 5% carbowax 20M, 6', 220°, 60 ml/min, R_t 8.5 min). IR (Fig. 58): (CCl_4): 2930, 2860 cm^{-1}, C=O 1735 cm^{-1}, C=C 1648, 1448 cm^{-1}, 1380, 1322, 1228, 1160, 1064, 926 cm^{-1}, C=C 860 cm^{-1}. PMR (Fig. 59): Me.C=CH, 3H, bs, 1.60 ppm; E-Me.C=C.COOMe, 3H, d, 1.88 ppm, J=2Hz; COOMe, 3H, ss, 3.62 ppm; CH=C, 1H, t, 5.22 ppm, J=7Hz; Me.C=CH, 1H, bm, 5.48 ppm, W_H=14Hz; C=CH.COOMe, 1H, bs, 5.58 ppm; CH_2, 16H, m, 1.2-2.8 ppm). Mass: m/e 276 (M^+, 44.4%), 163 (58.1%), 135 (75.4%), 114 (56.5%), 107 (89.5%), 95 (69.4%), 93 (53.2%), 81 (100%), 79 (89.5%), 67 (74.2%), 55 (66.5%). (Found: C, 78.6; H, 10.5. $C_{18}H_{28}O_2$ requires: C, 78.26; H, 10.15%).

dl-Methyl 7":13-cyclo-cis-10,11-epoxy-7-ethyl-3,11-dimethyl-trans-2,ξ-6-tridecadienoate; 7

A soln of m-Cl-$PhCO_3H$ (232.2 mg, 65%) in CH_2Cl_2 (10 ml) was added to a soln of E-ester 55 (276 mg) in CH_2Cl_2 (10 ml) at 0^o. The mixture was then left to stand overnight at 0^o in a refrigerator (preadjusted at 0^o). This was then diluted with CH_2Cl_2, washed with 5% Na_2CO_3 aq, washed, dried, and evaporated: colorless oil (254 mg) which was purified by preparative layer chromatography (PLC: silica gel, Tlc grade, 20 cm x 20 cm x 0.5 mm) developed by light petroleum: EtOAc, 18:2. Required cydononane analogue of JH-I (7, 70 mg) was obtained from a band at R_f 0.52. The starting E-ester 55 (36 mg) was recovered from a band at R_f 0.75. The diepoxide 57 (20 mg) was obtained from a band at R_f 0.23 (Tlc: light petroleum: C_6H_6, 18:1). The JH-mimic 7 showed the following properties: R_f 0.52 (Tlc: light petroleum: C_6H_6, 18:1). IR (Fig. 60): (CCl_4): 2930, 2860 cm^{-1}, C=O 1720 cm^{-1}, C=C 1645 cm^{-1}, 1432, 1378, 1356, 1325, 1275, 1245, 1220, 1145, 1035, 900, 812 cm^{-1}. PMR (Fig. 61): Me.C(—O—)C, 3H, ss, 1.20 ppm; Z-Me.C=C.COOMe, 3H, ss, 2.13 ppm; COOMe, 3H, ss, 3.62 ppm; CH=C, 1H, 5.12 ppm, W_H=12Hz; C=CH.COOMe, 1H, bs, 5.58 ppm; CH, CH_2, Me.C(—O—)CH, 16H, m, 1.24-3.0 ppm. Mass (Fig. 61A): m/e 292 (M^+, 4.3%), 161 (91.5%), 135 (63.8%), 121 (53.2%), 114 (59.6%), 107 (59.6%), 95 (89.4%), 93 (78.7%), 80(100%), 78 (70.2%), 67(76.6%), 55(72.3%). (Found: C, 74.2; H, 9.7. $C_{18}H_{28}O_3$ requires: C, 73.97; H, 9.59%).

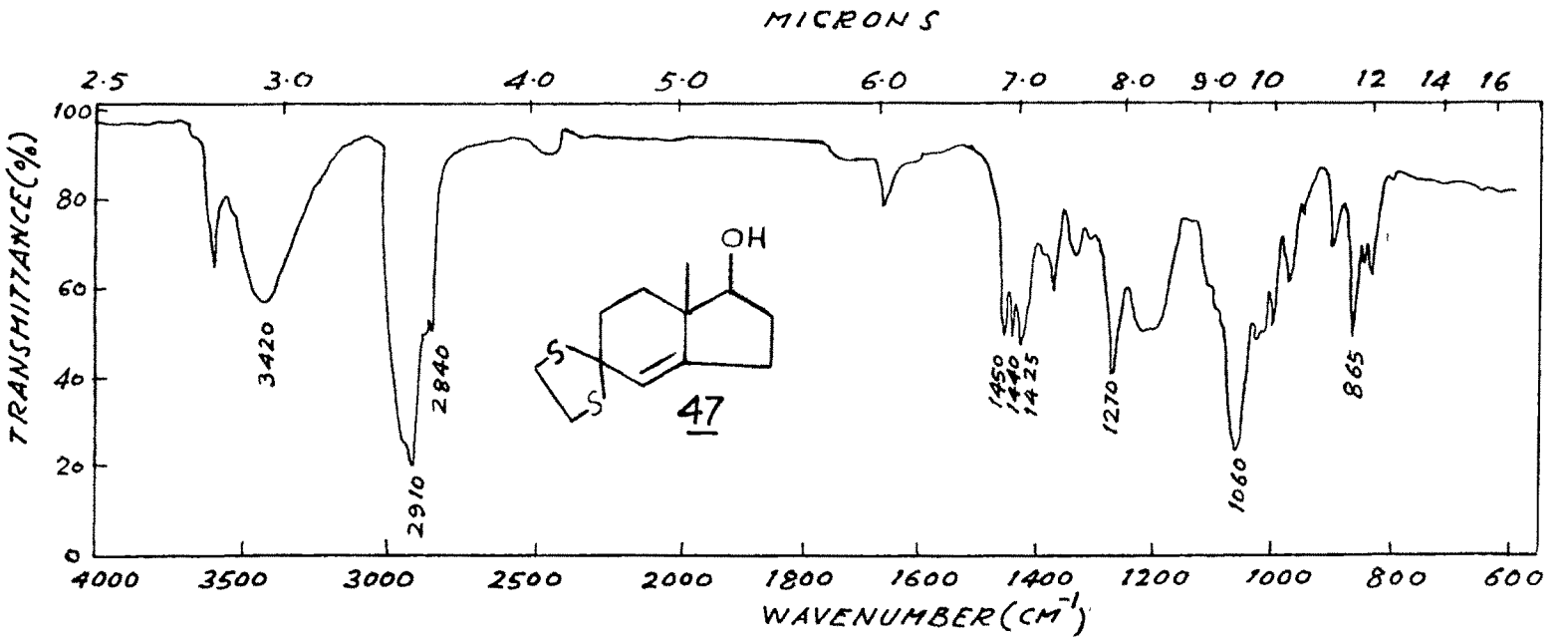


FIG.40 - IR SPECTRUM OF 3,3-ETHYLENEDITHIO-7β-HYDROXY-6β-METHYL-BICYCLO(4,3,0) NON-1-ENE; 47

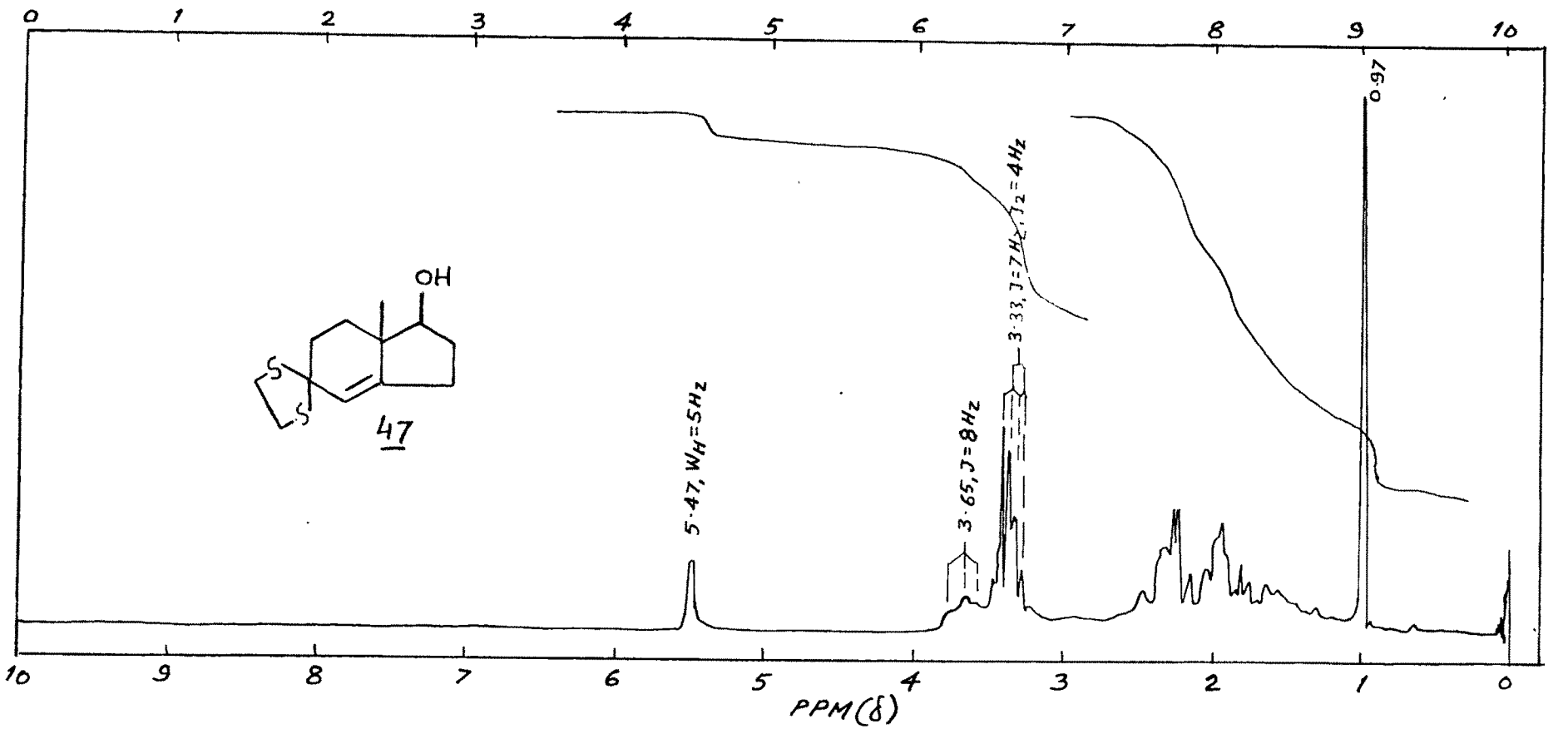


FIG.41 - NMR SPECTRUM OF 3,3-ETHYLENEDITHIO-7β-HYDROXY-6β-METHYL-BICYCLO(4,3,0) NON-1-ENE, 47

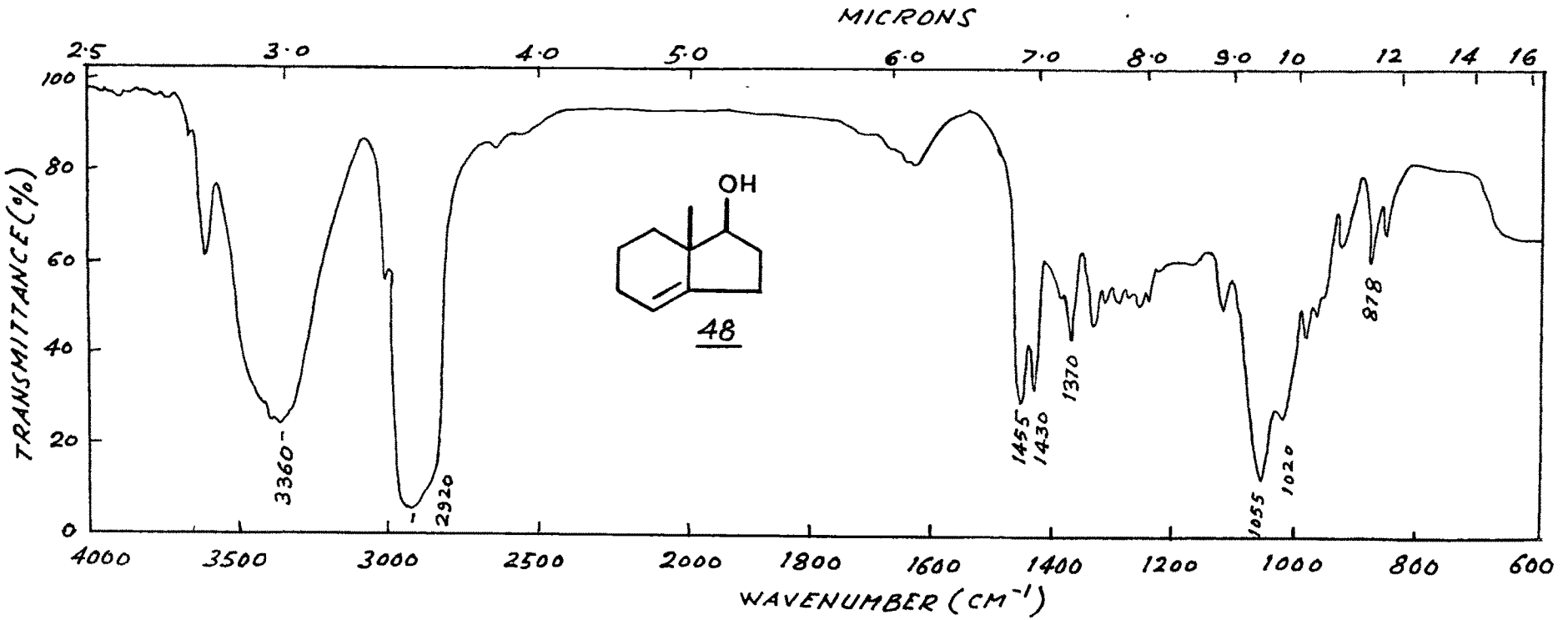


FIG. 42 - IR SPECTRUM OF 7β-HYDROXY-6β-METHYL-BICYCLO (4,3,0) NON-1-ENE; 48

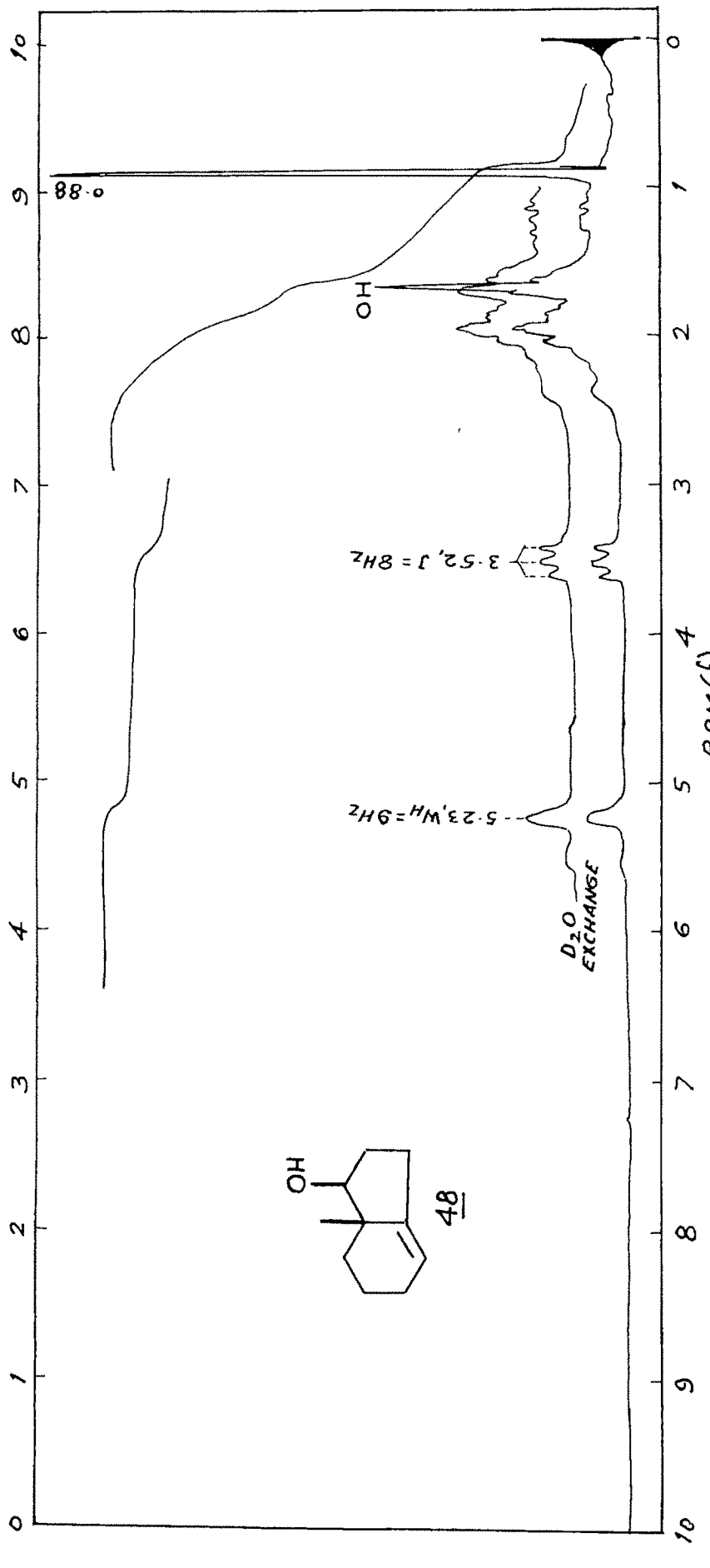


FIG. 43 - NMR SPECTRUM OF 7β-HYDROXY-6β-METHYL-BICYCLO (4,3,0) NON-1-ENE, 48

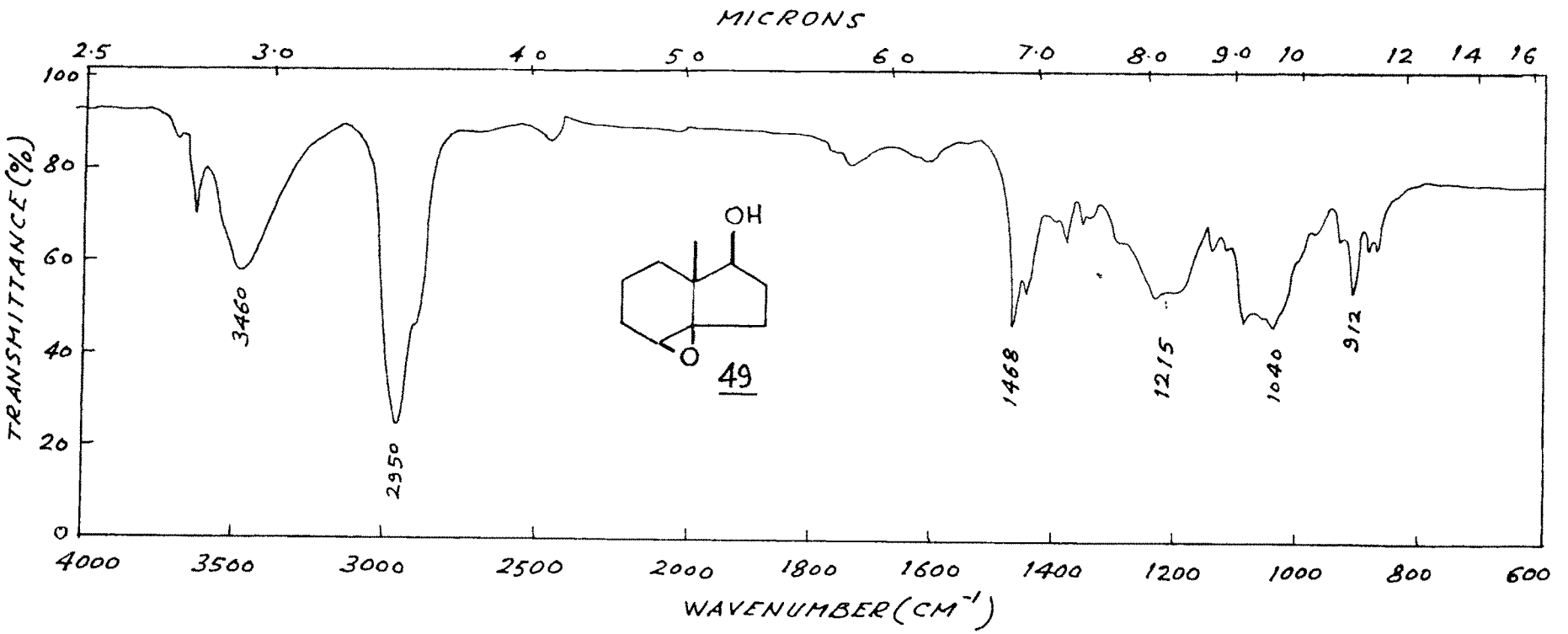


FIG. 44 - IR SPECTRUM OF 1,2-β-EPOXY-7β-HYDROXY-6β-METHYL-BICYCLO (4,3,0) NONANE, 49

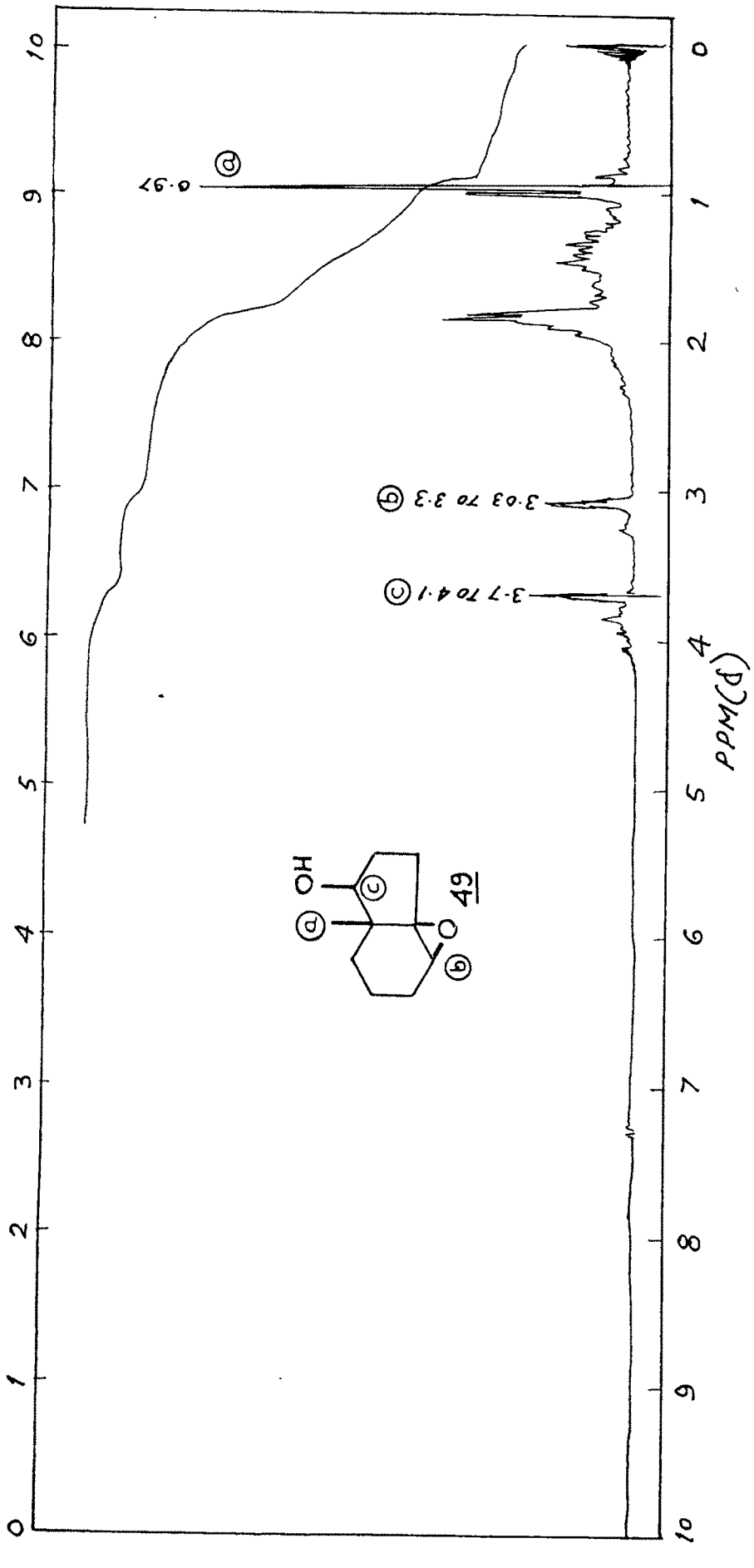


FIG.45- NMR SPECTRUM OF 1,2-β-EPOXY-7β-HYDROXY-6β-METHYL-BICYCLO(4,3,0) NONANE; 49

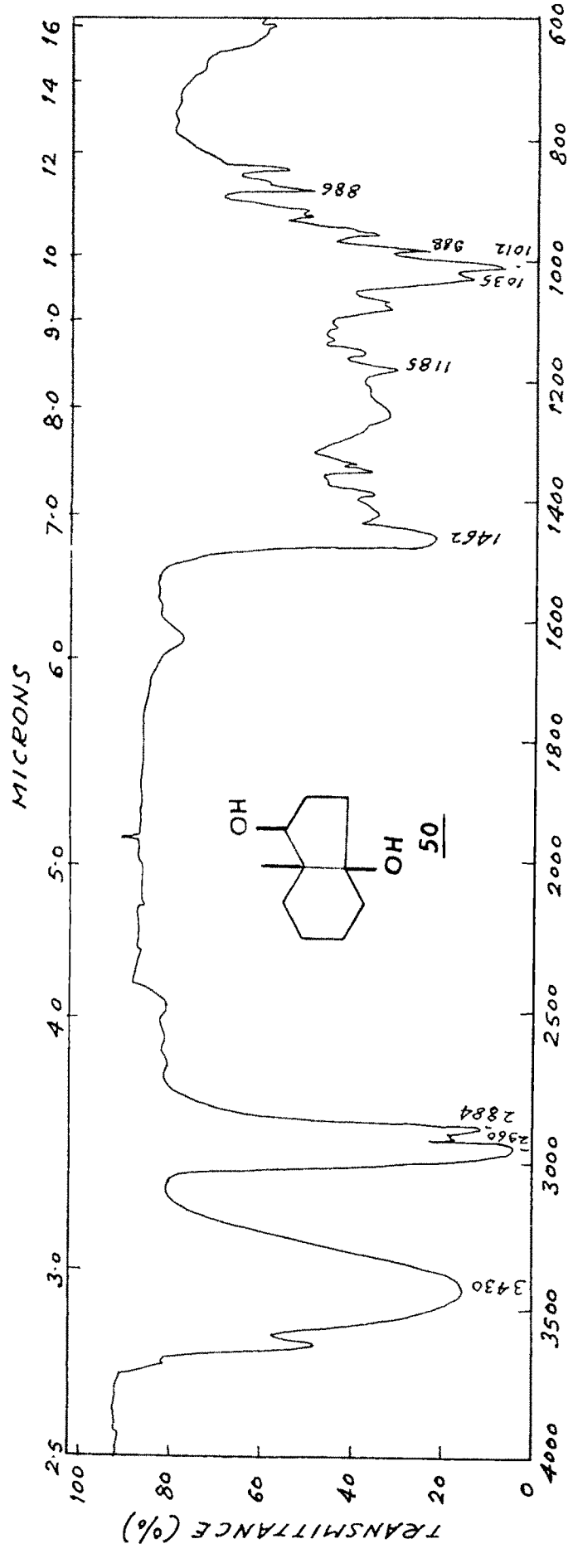


FIG. 46 - IR SPECTRUM OF 1β,7β-DIHYDROXY-6β-METHYL-BICYCLO(4,3,0) NONANE; 50

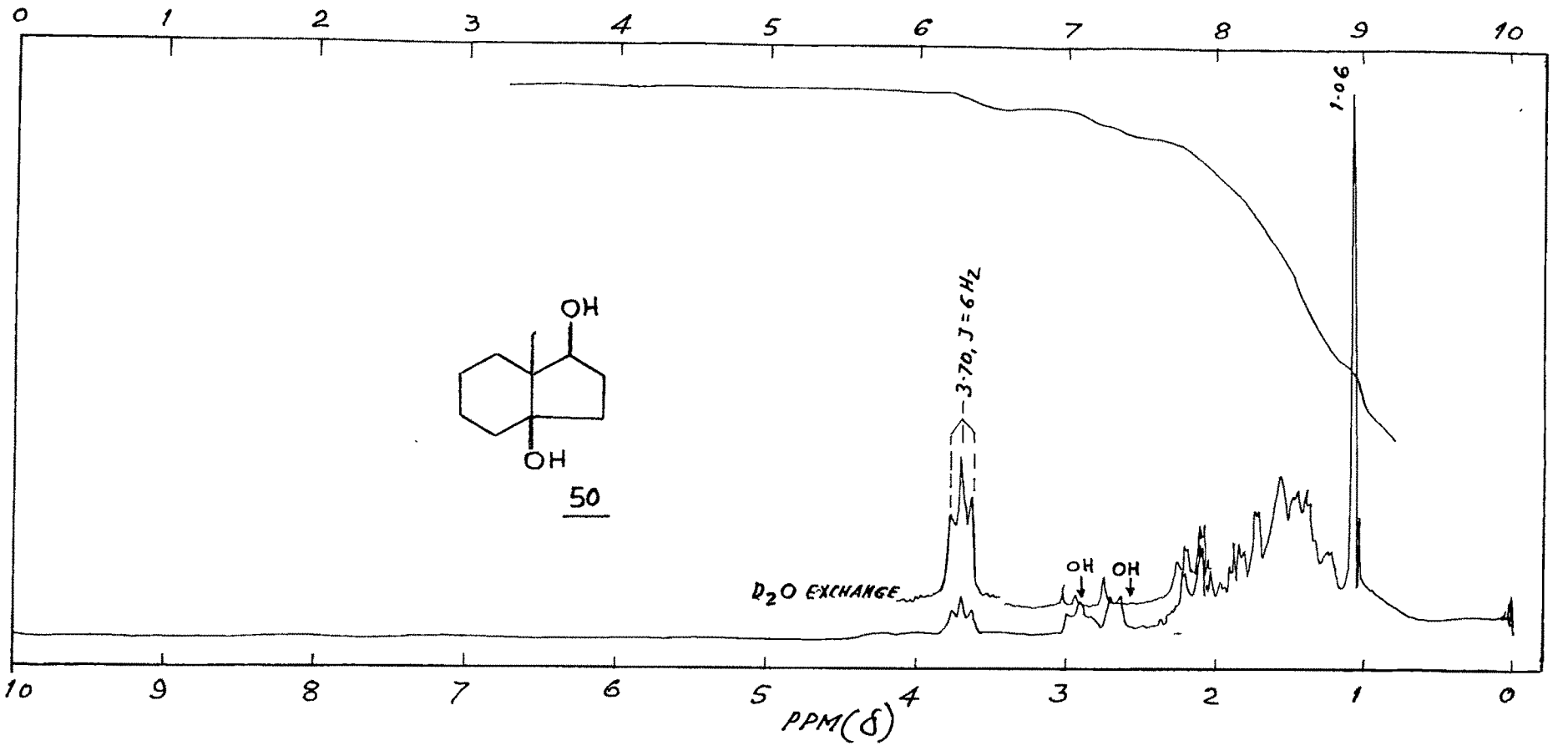


FIG.47- NMR SPECTRUM OF 1β,7β-DIHYDROXY-6β-METHYL-BICYCLO(4,3,0) NONANE; 50

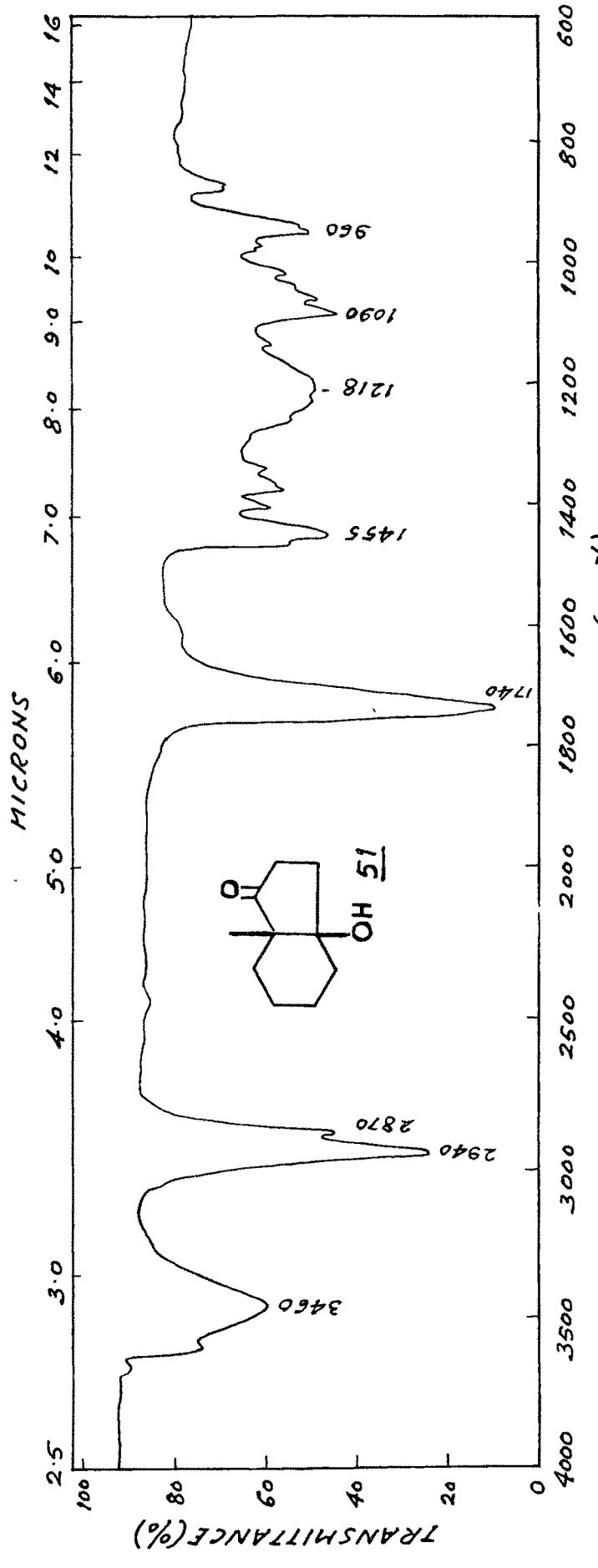


FIG. 48 - IR SPECTRUM OF 1β - HYDROXY - 6β - METHYL - BICYCLO(4,3,0)NONAN - 7 - ONE; 51

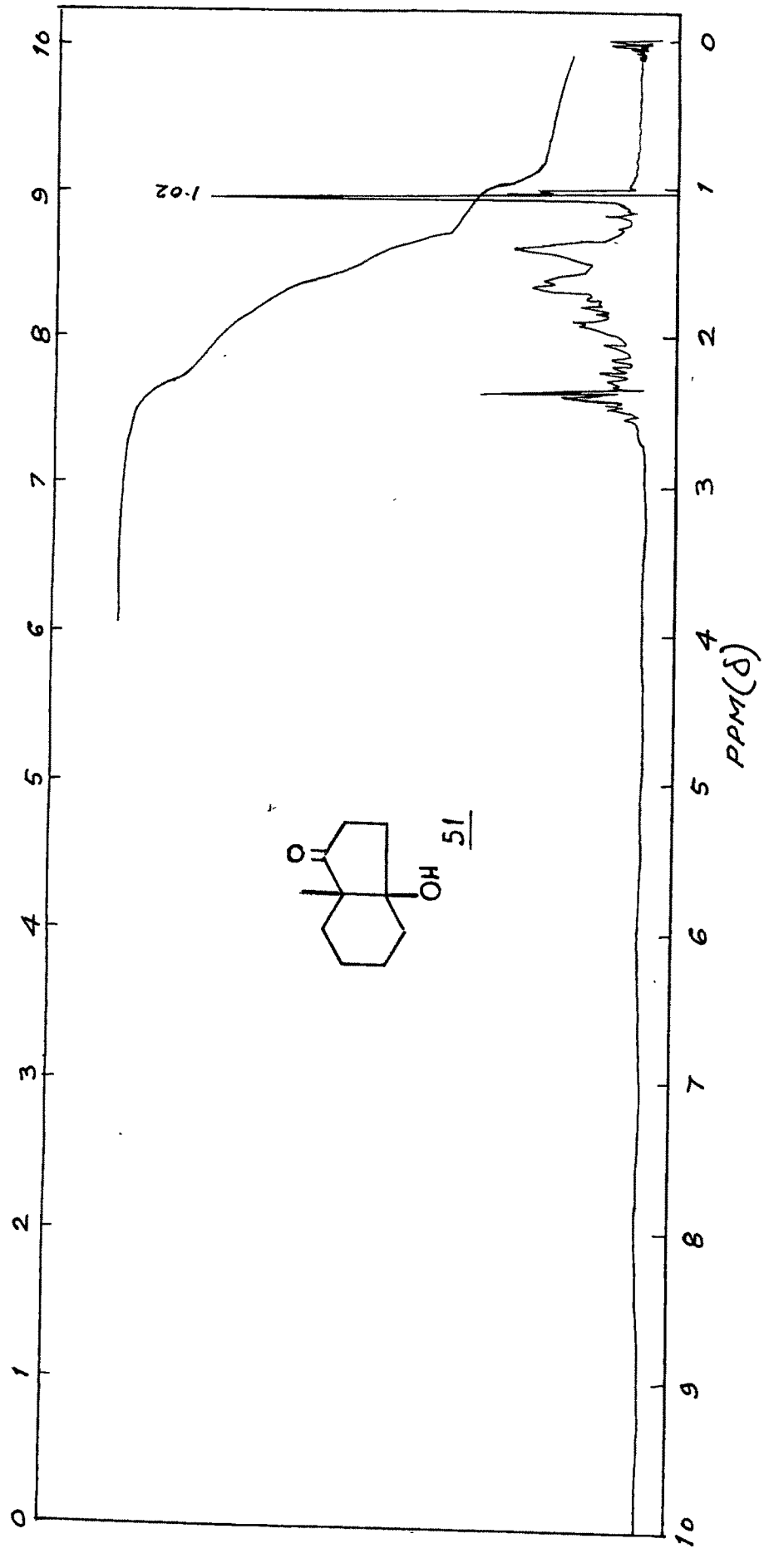


FIG.49 - NMR SPECTRUM OF 1β - HYDROXY - 6β - METHYL - BICYCLO(4,3,0) NONAN - 7 - ONE; 51

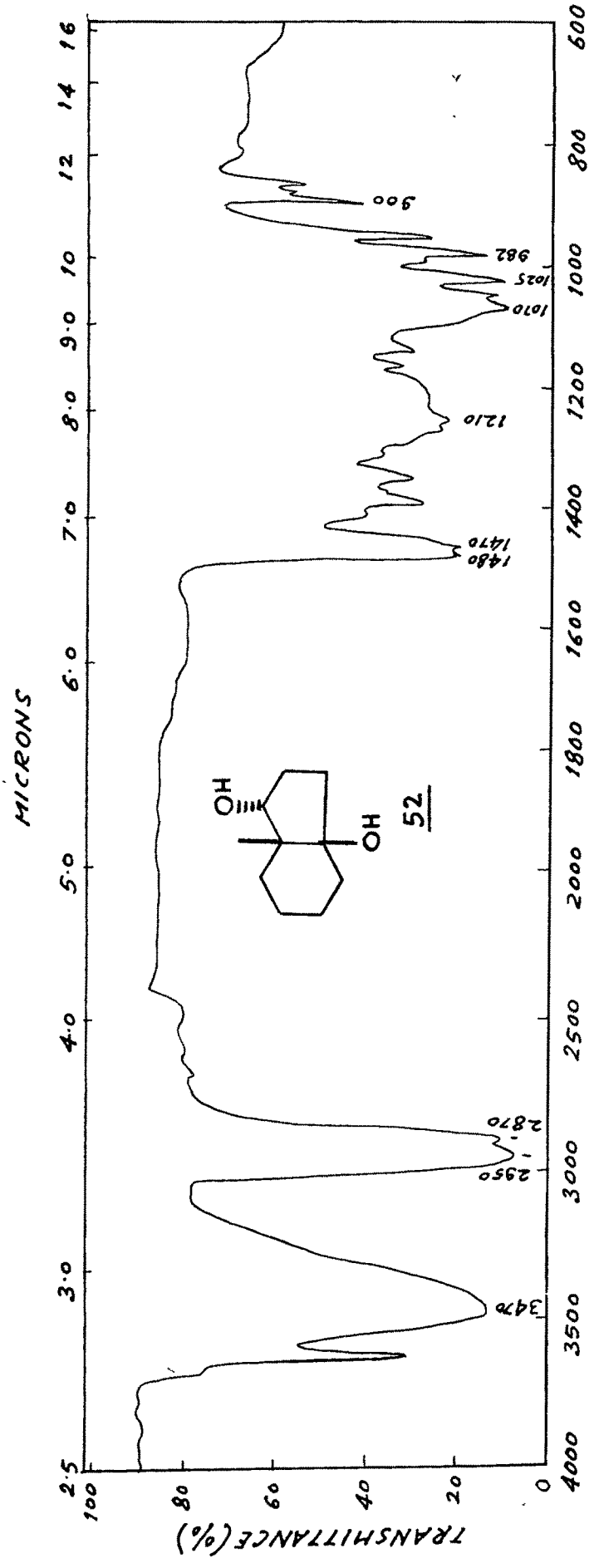


FIG.50 - IR SPECTRUM OF 1β,7α-DIHYDROXY-6β-METHYL-BICYCLO(4,3,0)NONANE; 52

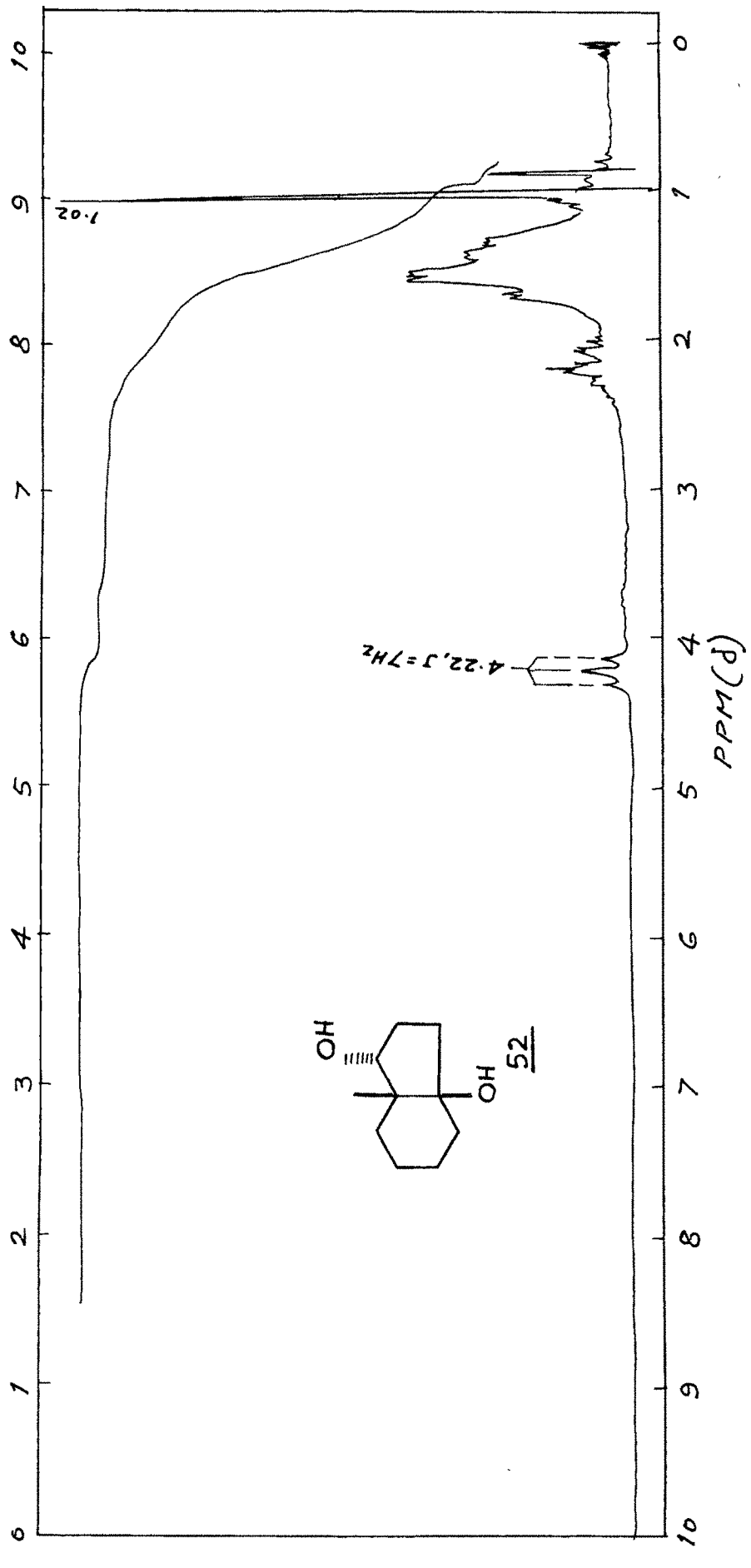


FIG.51 - NMR SPECTRUM OF 1β,7α-DIHYDROXY-6β-METHYL-BICYCLO(4,3,0) NONANE; 52

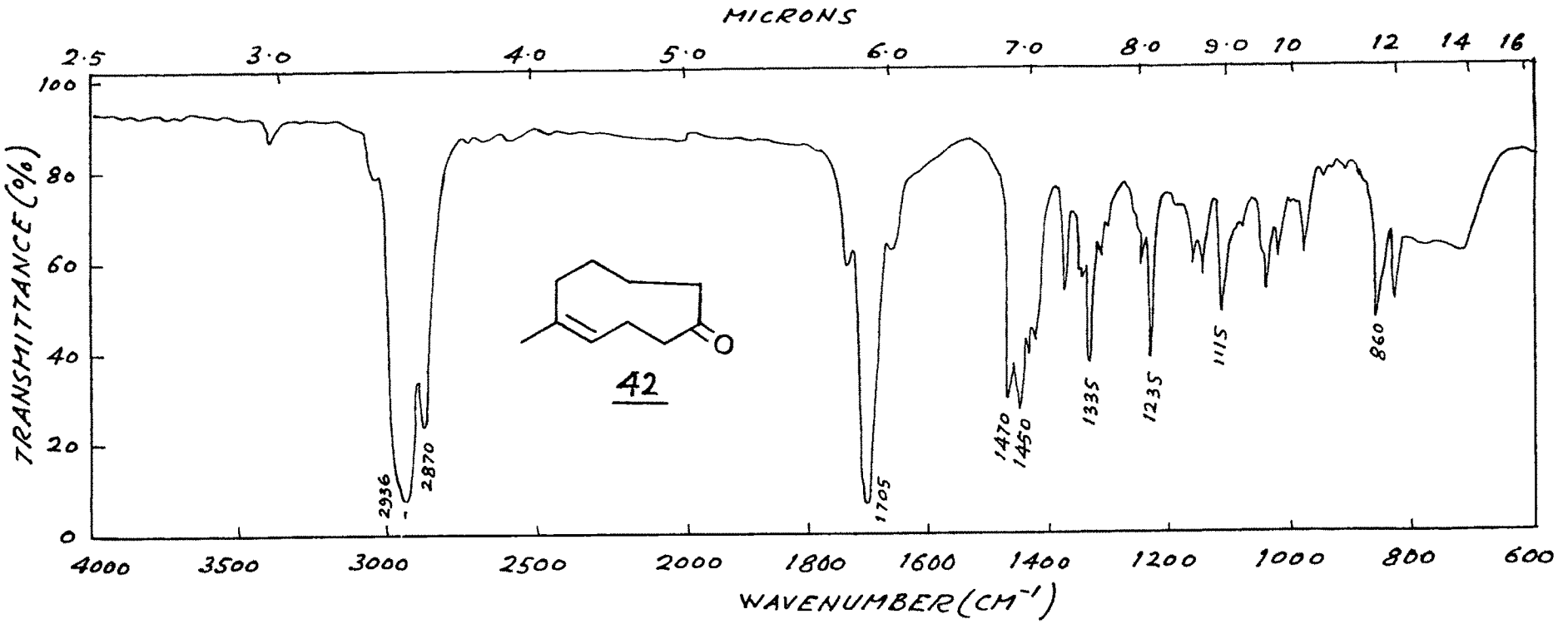


FIG. 52 - IR SPECTRUM OF 5-METHYL-CYCLONON-4(Z)-EN-1-ONE; 42

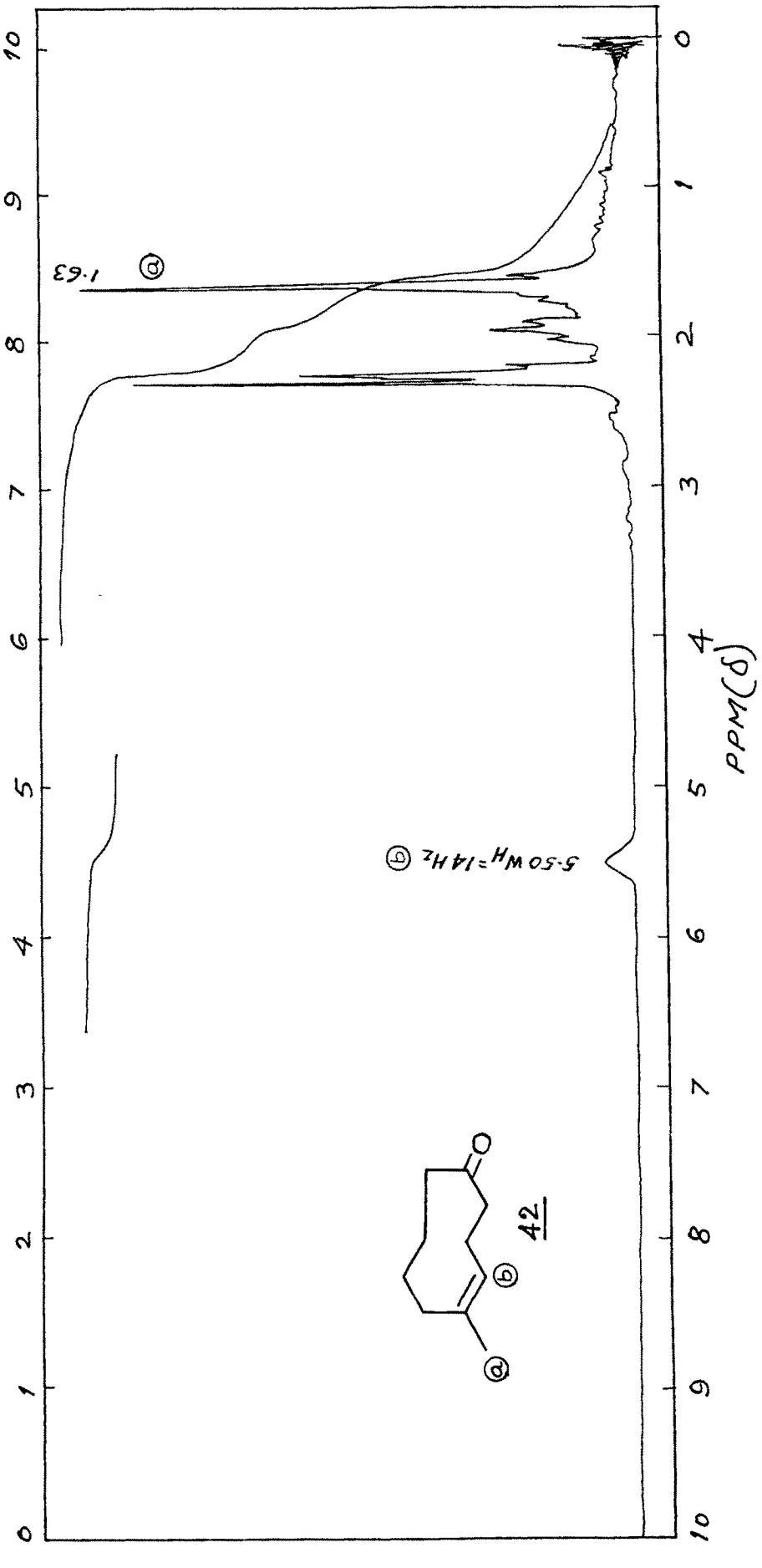


FIG. 53- NMR SPECTRUM OF 5-METHYL-CYCLONON-4(Z)-EN-1-ONE; 42

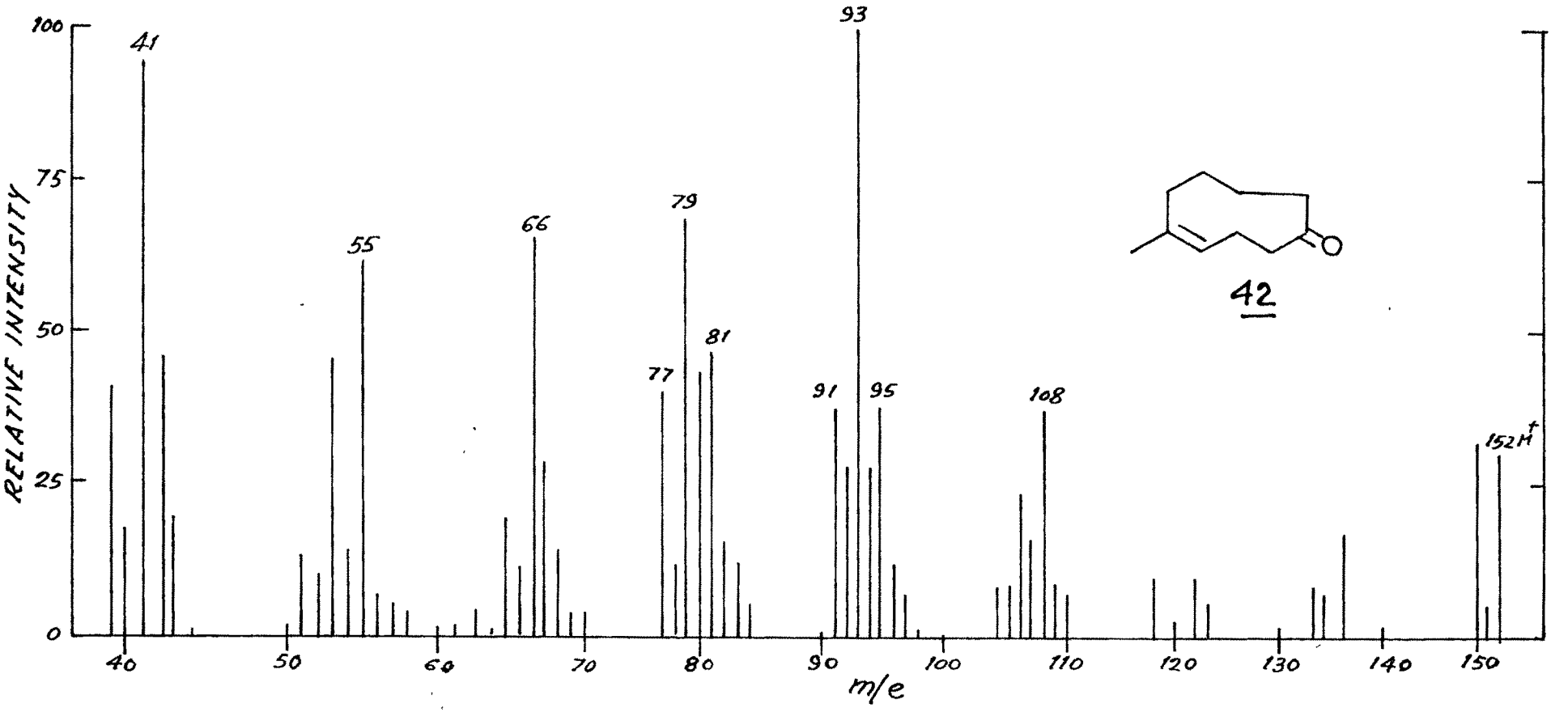


FIG. 53A - MASS SPECTRUM OF 5-METHYL-CYCLONON-4(Z)-EN-1-ONE; 42

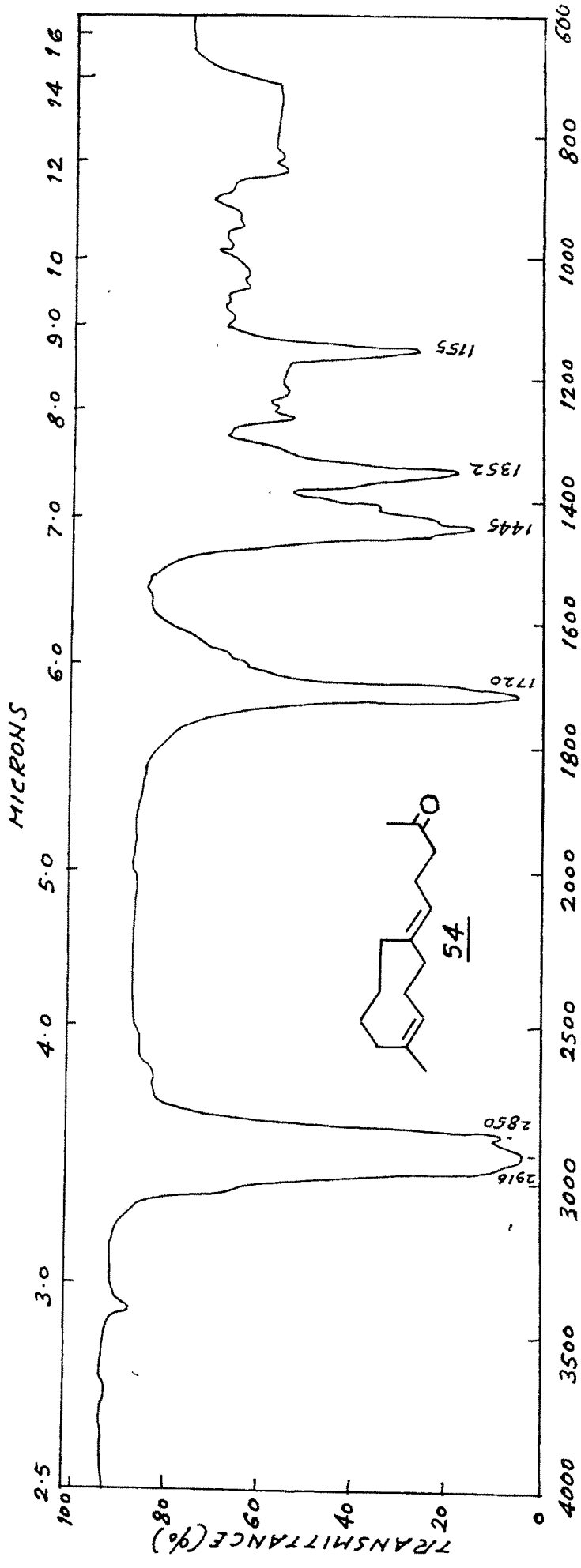


FIG.54 - IR SPECTRUM OF 6":12-CYCLO-10-METHYL-6-ETHYL-Σ-5, CIS-9-DODECADIENE-2-ONE; 54

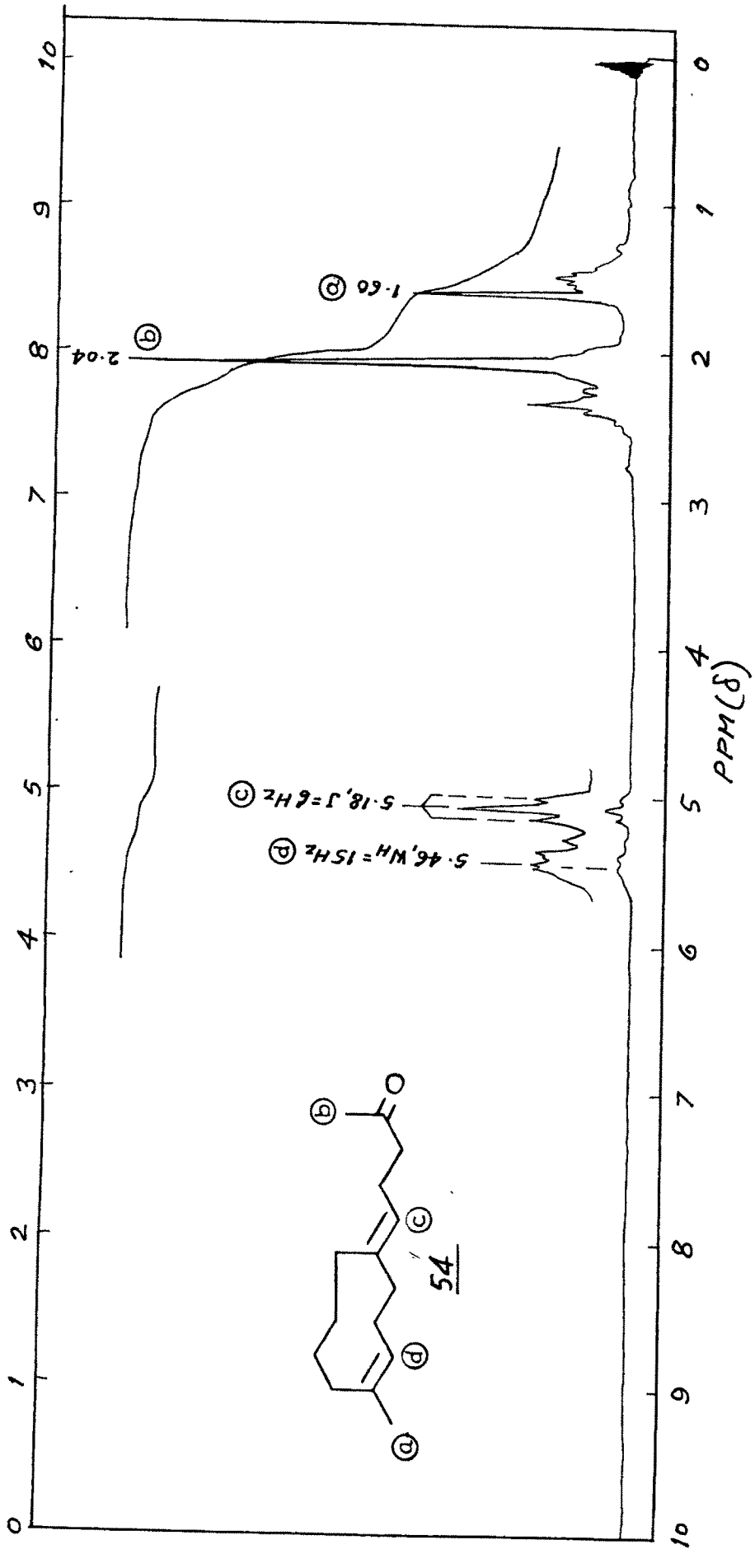


FIG. 55 NMR SPECTRUM OF 6":12-CYCLO-10-METHYL-6-ETHYL-E-5, CIS-9-DODECADIENE-2-ONE; 54

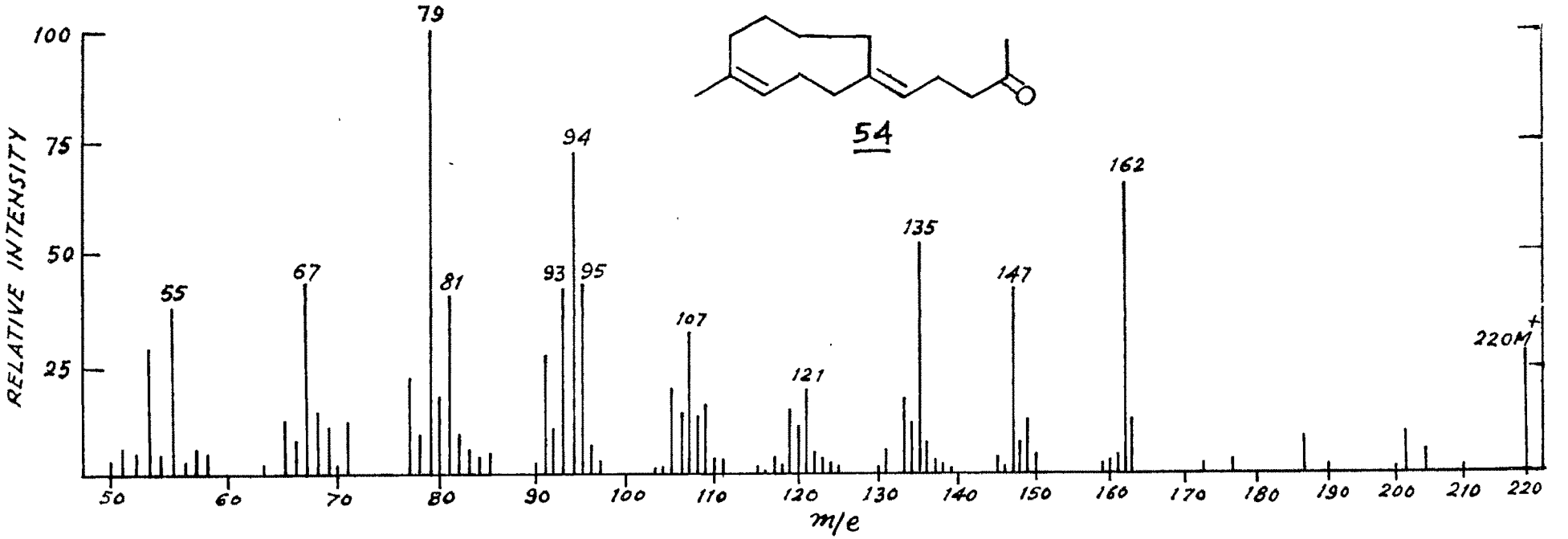


FIG. 55A - MASS SPECTRUM OF 6'':12-CYCLO-10-METHYL-6-ETHYL-$\underline{\xi}$-5, CIS-9-DODECADIENE-2-ONE; 54

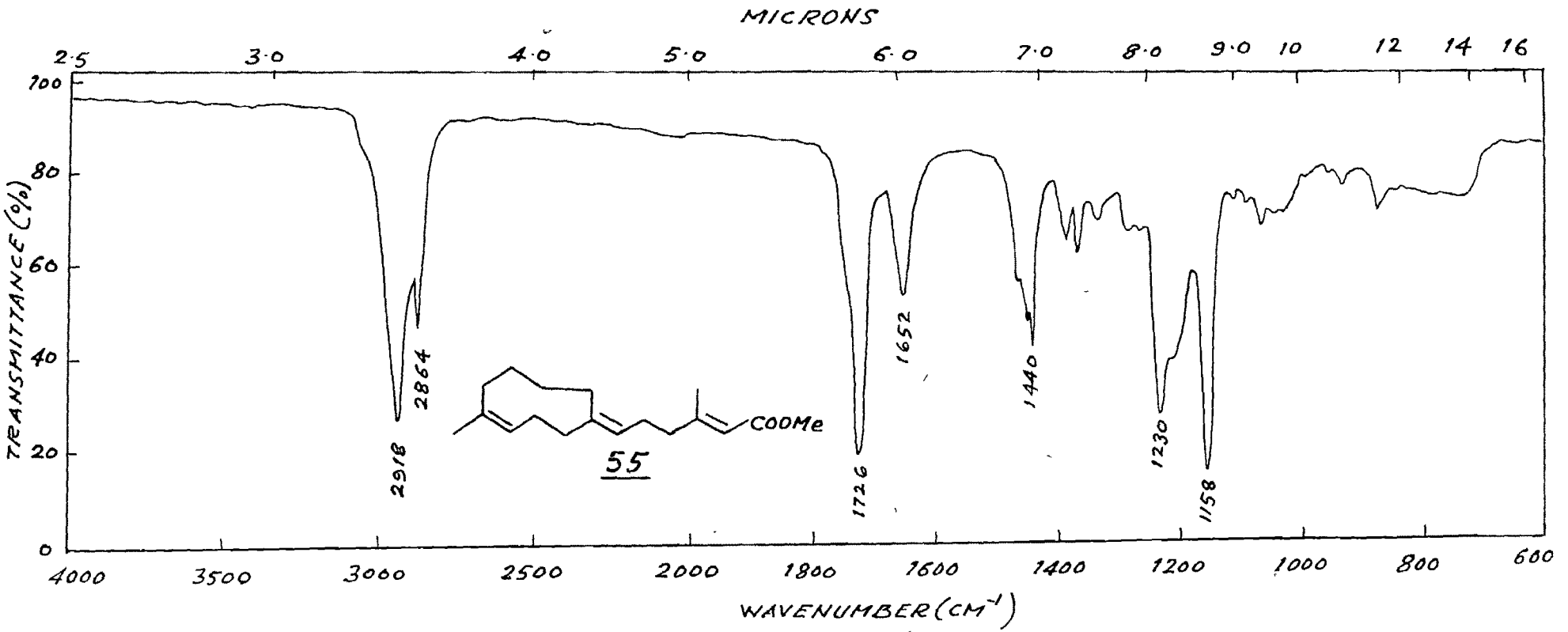


FIG. 56 - IR SPECTRUM OF METHYL 7":13-CYCLO-7-ETHYL-3,11-DIMETHYL-TRANS-2,§-6,CIS-10-TRIDECATRIENOATE; 55

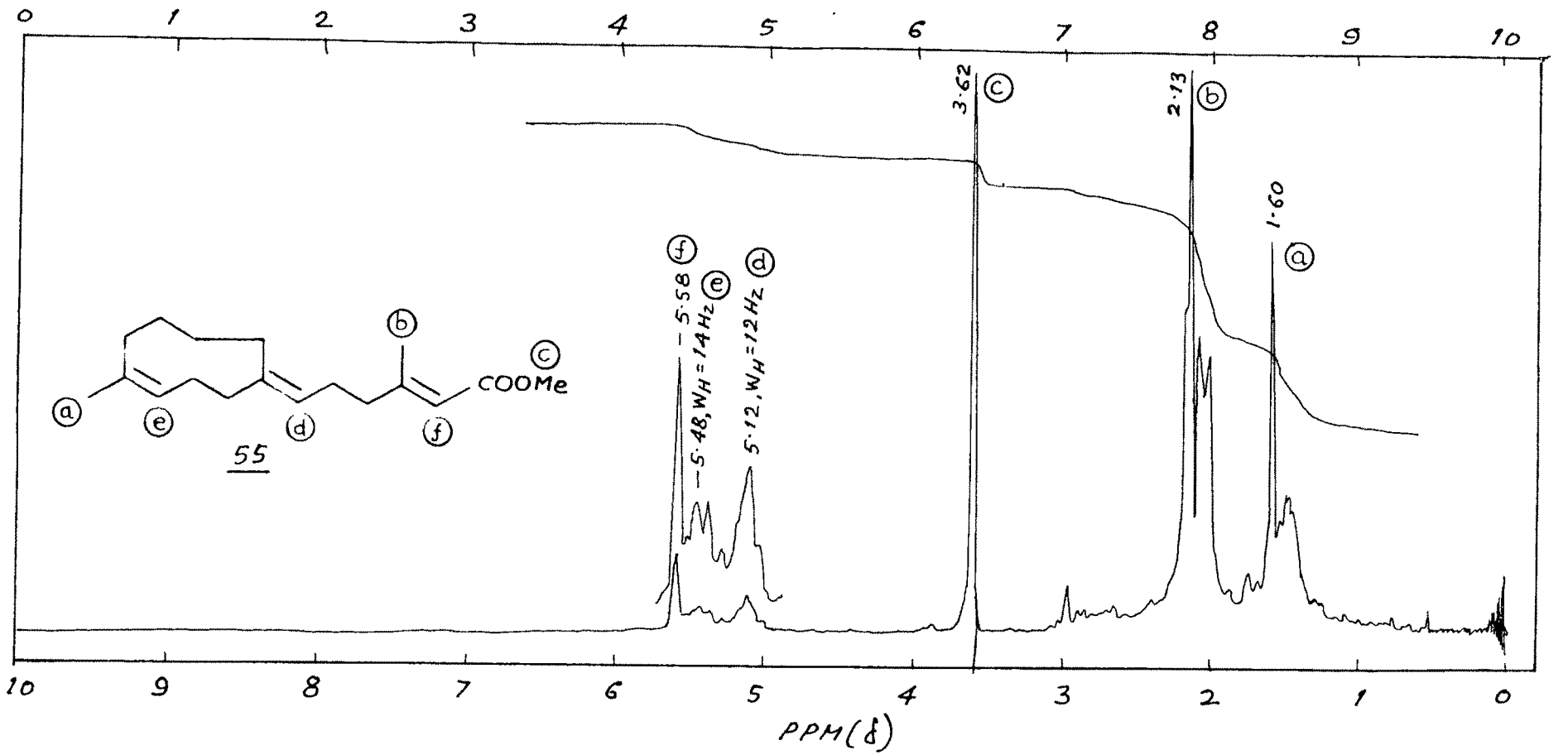


FIG.57 - NMR SPECTRUM OF METHYL 7":13 - CYCLO - 7 - ETHYL - 3, 11 - DIMETHYL - TRANS - 2, E - 6, CIS - 10 - TRIDECATRIENOATE; 55

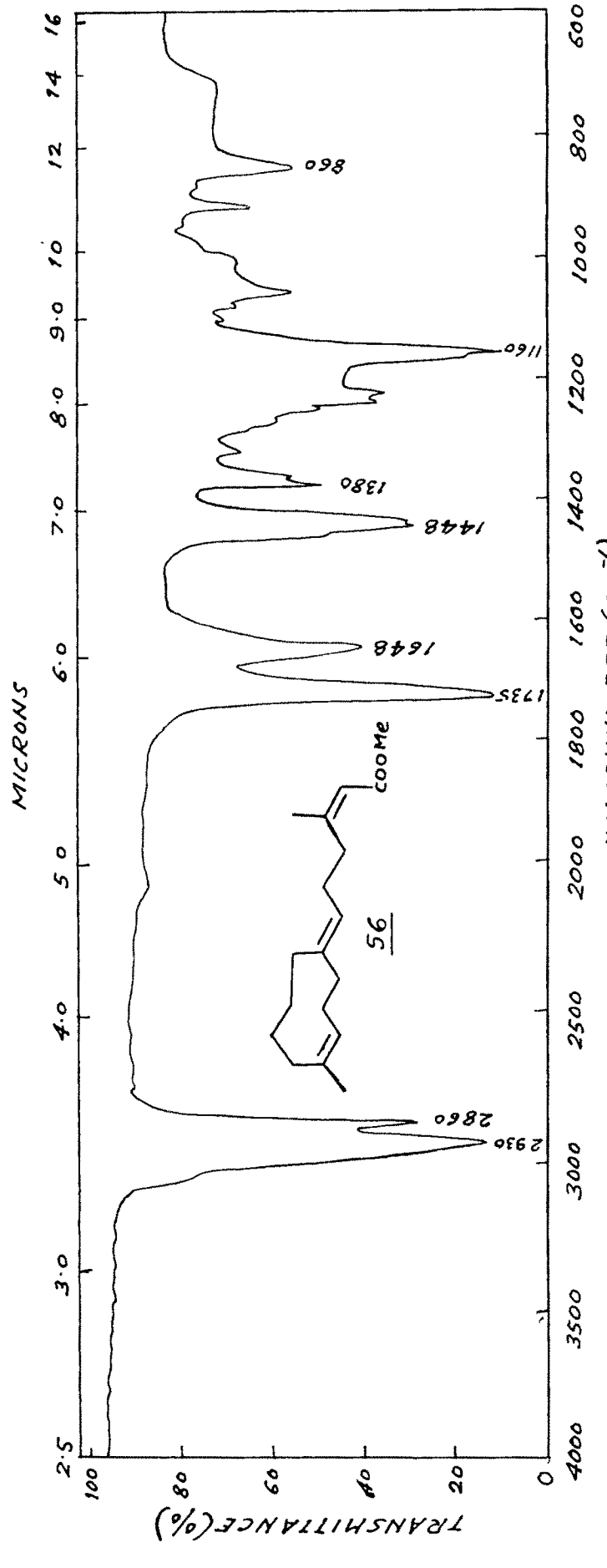


FIG. 58 - IR SPECTRUM OF METHYL 7": 13-CYCLO-7-ETHYL-3,11-DIMETHYL-CIS-2, ξ-6, CIS-10-TRIDECATRIENOATE; 56

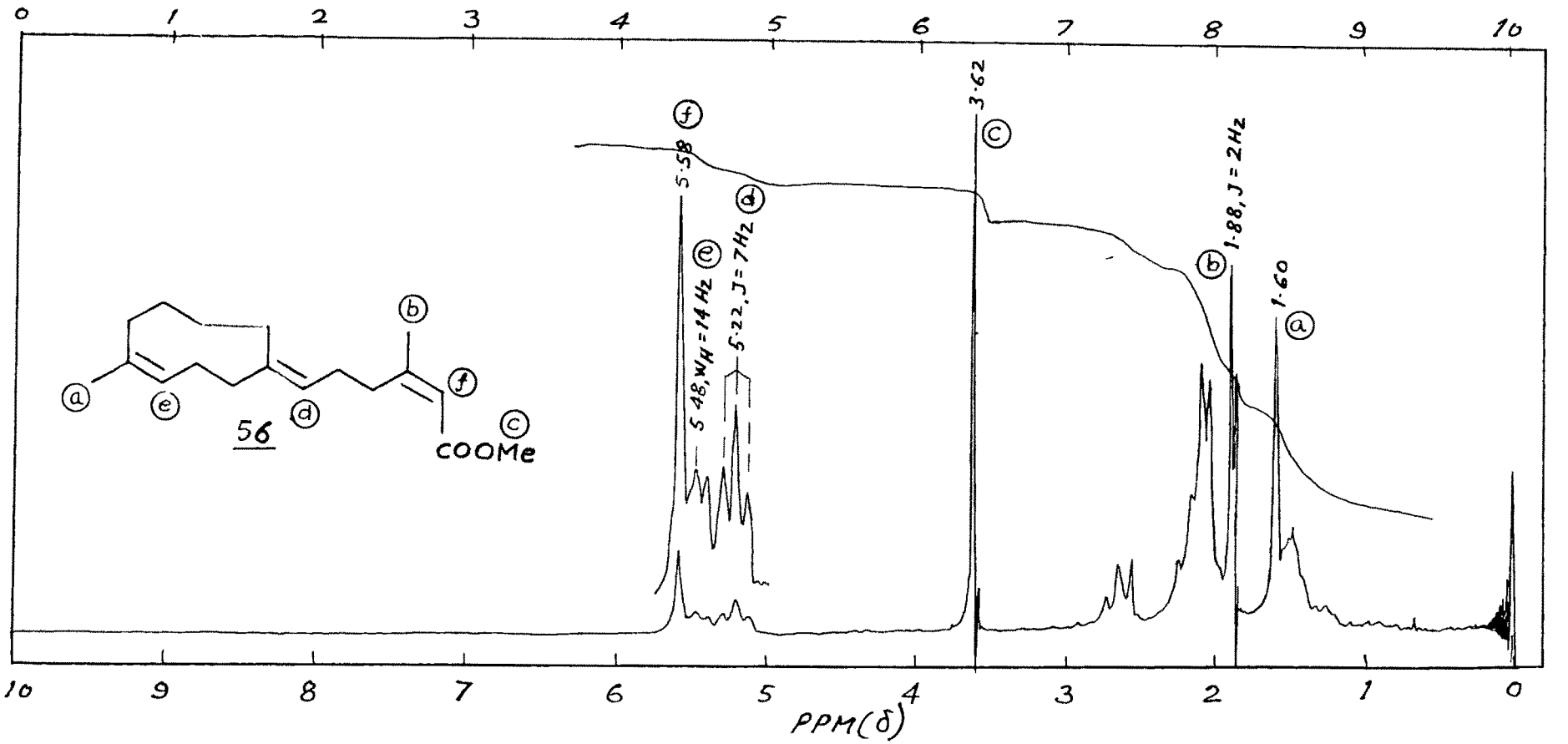


FIG. 59 - NMR SPECTRUM OF METHYL 7"13 - CYCLO - 7 - ETHYL - 3, 11 - DIMETHYL - CIS - 2, E - 6, CIS - 10 - TRIDECATRIENOATE; 56

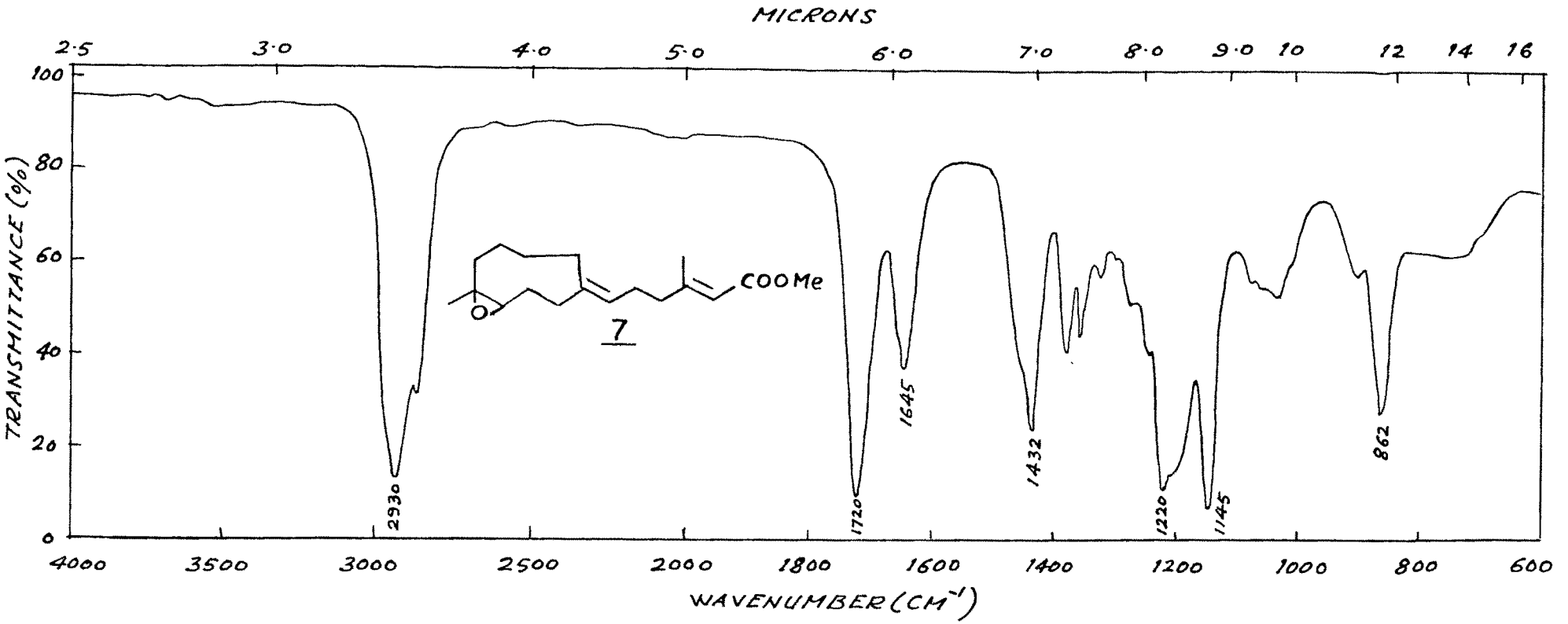


FIG. 60 - IR SPECTRUM OF DL-METHYL 7":13-CYCLO-CIS-10, 11-EPOXY-7-ETHYL-3, 11-DIMETHYL-TRANS-2, §-6-TRIDECADIENOATE; 7

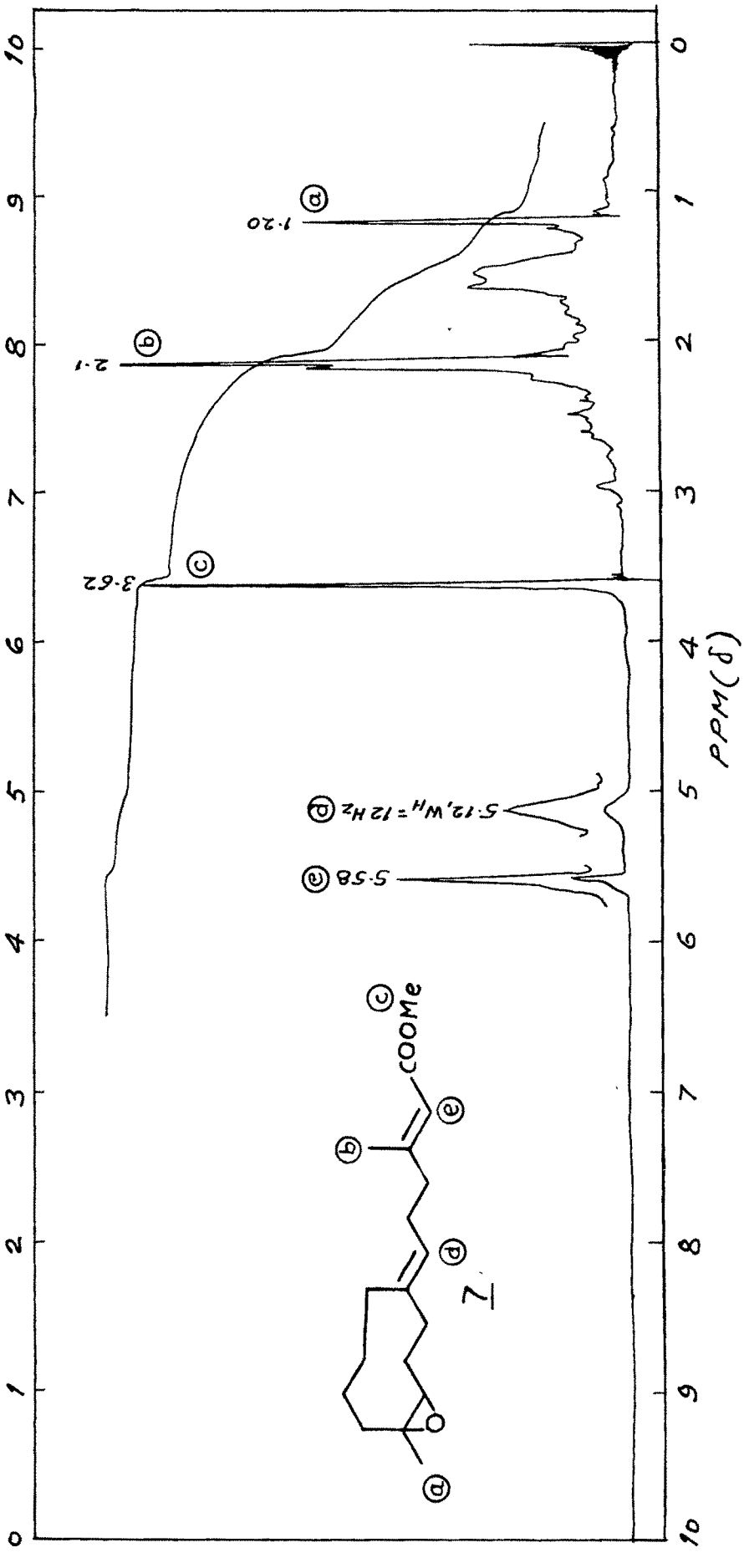


FIG. 61 - NMR SPECTRUM OF DL-METHYL 7":13-CYCLO-CIS-10,11-EPOXY-7-ETHYL-3,11-DIMETHYL-TRANS-2,E-6-TRIDECADIENOATE; Z

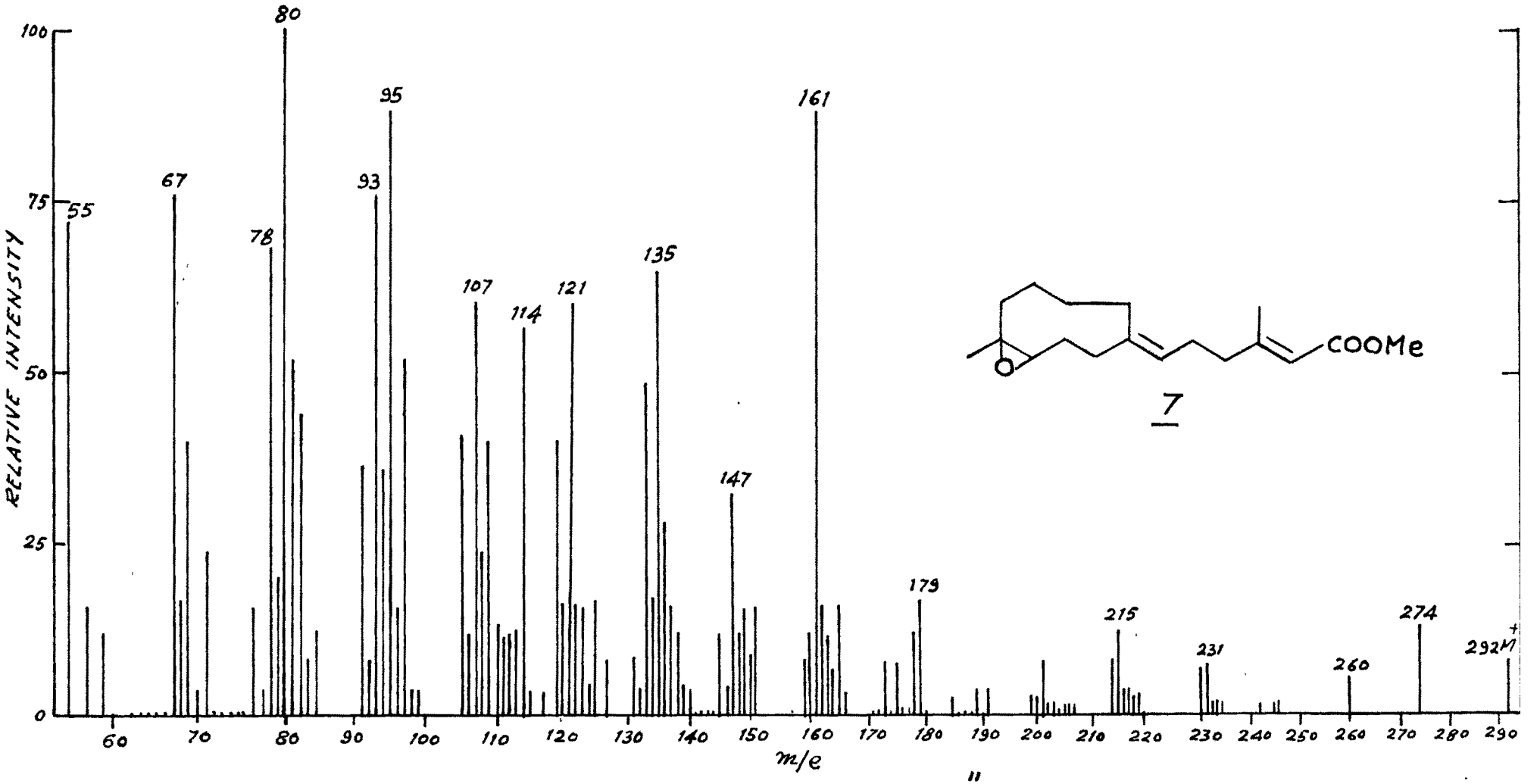


FIG. 61A - MASS SPECTRUM OF DL-METHYL 7:13-CYCLO-CIS-10,11-EPOXY-7-ETHYL-3,11-DIMETHYL-TRANS-2,E-6-TRIDECADIENOATE; 7

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