CHAPTER—II

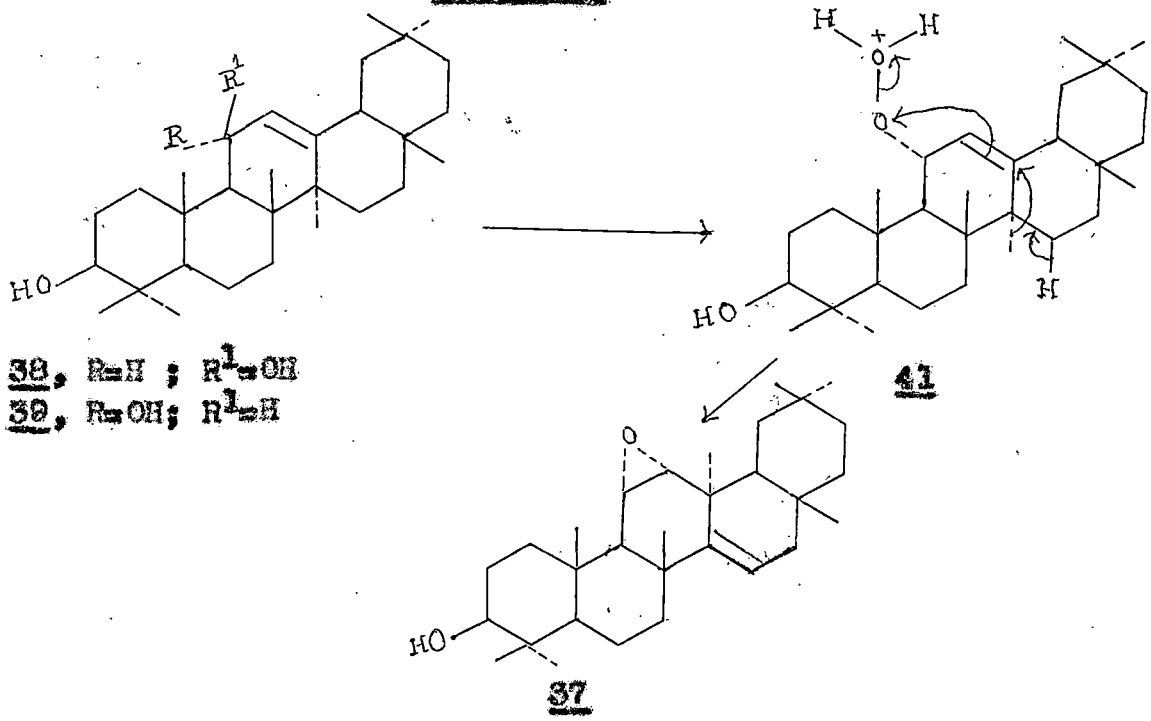
RESULTS AND DISCUSSION

SECTION—A:

Action of hydrogen peroxide on olean-12,15-dien-3,11-diol:

In order to synthesize partially some derivatives of triterpenoids like 16-hydroxy taraxerol 75 and multiflorenol derivative 74 from taraxeryl acetate we followed the methods of Corey et al[23]. They synthesized epoxy taraxerol 37, from both the olean-12-en-3β, 11β-diol 38 and olean-12-en-3β-11α-diol 40, by treatment with a mixture of hydrogen peroxide and selenious acid in t-butyl alcohol. They got the same epoxide from both the diol and not the epimeric one. This fact suggested that the formation of same epoxide 37 from the C—11 isomeric diols must proceed by C—11—O bond cleavage with the formation of the same c, 11,12,13 allylic cation which then formed the hydroperoxide 41, which can be shown in Scheme—8. The hydroperoxide 41

Scheme—8



38, R=H ; R^1=OH
39, R=OH; R^1=H

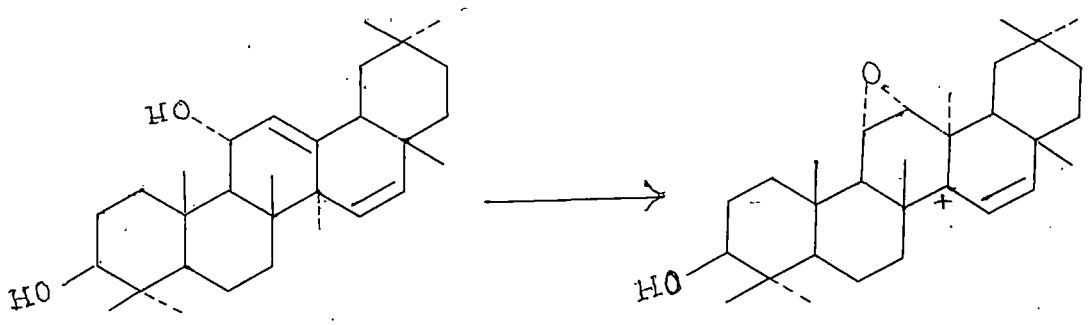
41

37

in turn undergoes O—O fission and carbon rearrangement to afford 37. They have reported that this type of rearrangement occurred in presence of para toluenesulphonic acid also.

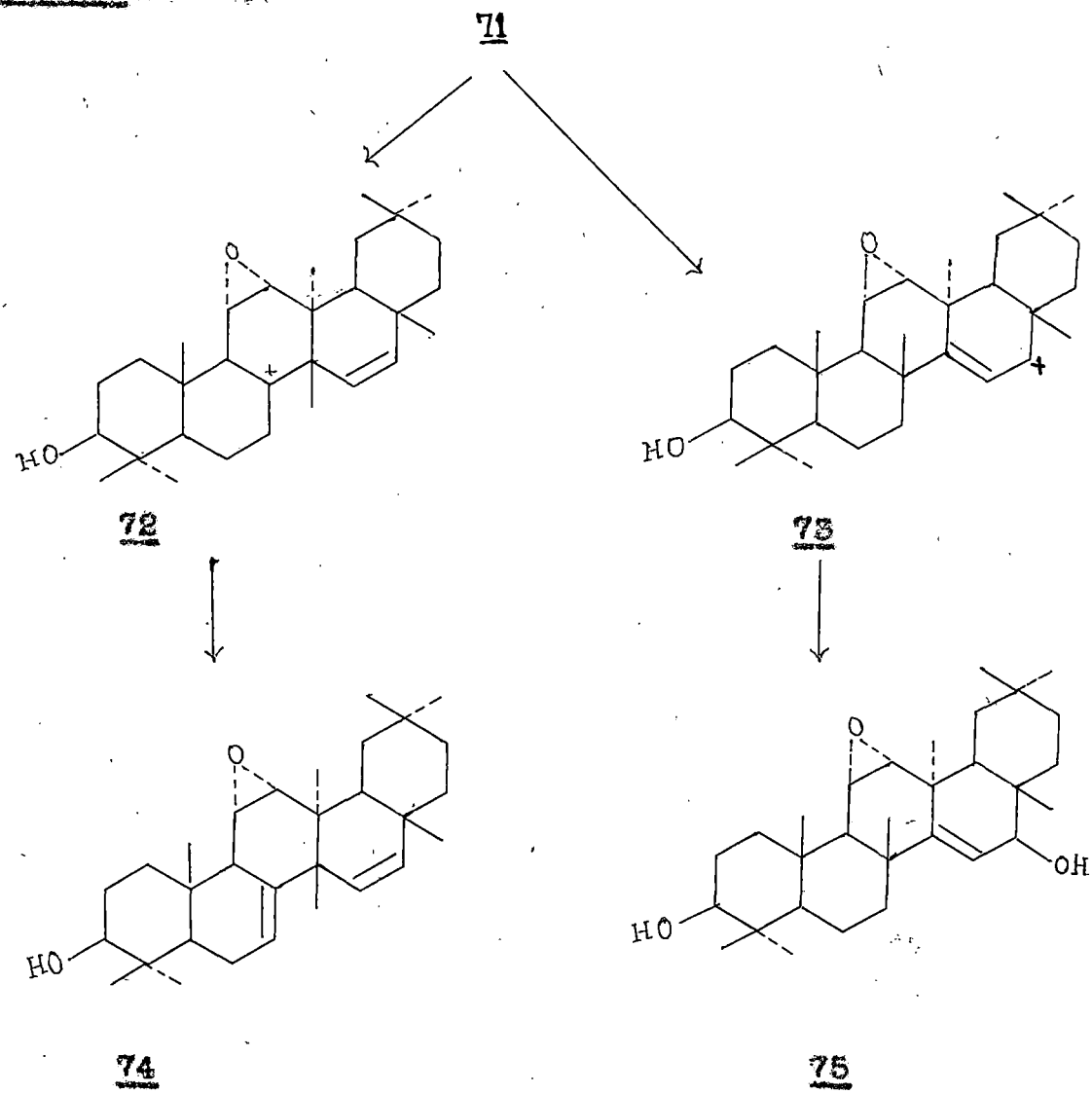
We assumed that this type of reaction could also be carried out on olean-12,15-dien-3,11-diol 70, which could be synthesized from taraxeryl acetate that will be discussed later on. The compound 70 would produce the epoxide with the allylic cation 71. The intermediate would further isomerize to produce the allylic cation 73, by the migration of C-15-16 double bond. The cation would undergo neucleophillic attack by OH^- ion to produce a 16-hydroxy-taraxerol derivative 75. In the other way the cation 71 would isomerize by the migration of C—8 methyl group to C—14 position to produce another cation 72 which was expected to elliminate a C—7 proton to give a multiflorenol derivative 74. The Scheme is given below (Scheme—9):

Scheme—9



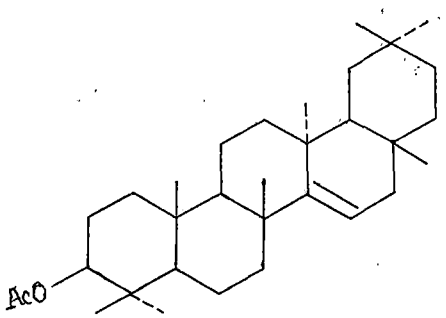
70 71

Scheme—9(contd.)



We have planned the scheme like above but when we carried out the reaction, the product which we actually got were quite different from the assumed ones, which are discussed in this section. First, the preparation of olean, 12,15-dien-3,11-diol 70, from taraxeryl acetate 76 and then the reaction of hydrogen peroxide in presence of para toluene-sulphonic acid on 70 is discussed.

When taraxeryl acetate 76 was treated with N-bromo-succinimide in presence of dimethylsulfoxide in a chloroform solution in dark for 12 hours, it furnished a solid which after crystallization gave a solid 77, $C_{32}H_{51}O_2Br$, m.p. 180—82°, $[\alpha]_D$ +47.4°. No UV absorption was observed for the compound in the region 220—350 nm. IR spectrum (Fig.1) of the compound showed two peaks at 1720 and 1250 cm^{-1} that revealed the compound contained one acetate functional group. PMR spectrum (Fig.2) of the compound showed that there was multiplet at 5.3 ppm for only one proton for $>C{=}C<_{H}$. Another multiplet centred at 4.53 ppm was due to one proton in H—C—O—COCH_3. The compound gave a multiplet at the region 4.3 ppm for one proton of H—C—Br. The singlet at 2.09 ppm was due to the three protons of —O—CO—CH_3. On the basis of IR and NMR spectrum, the structure 77 was assigned for the bromo compound. The structure



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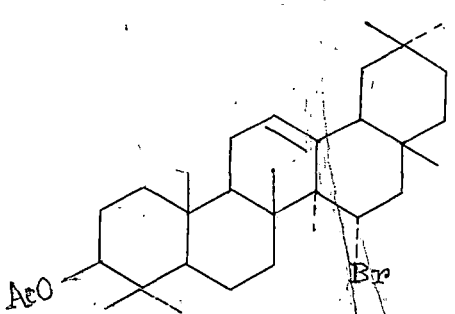

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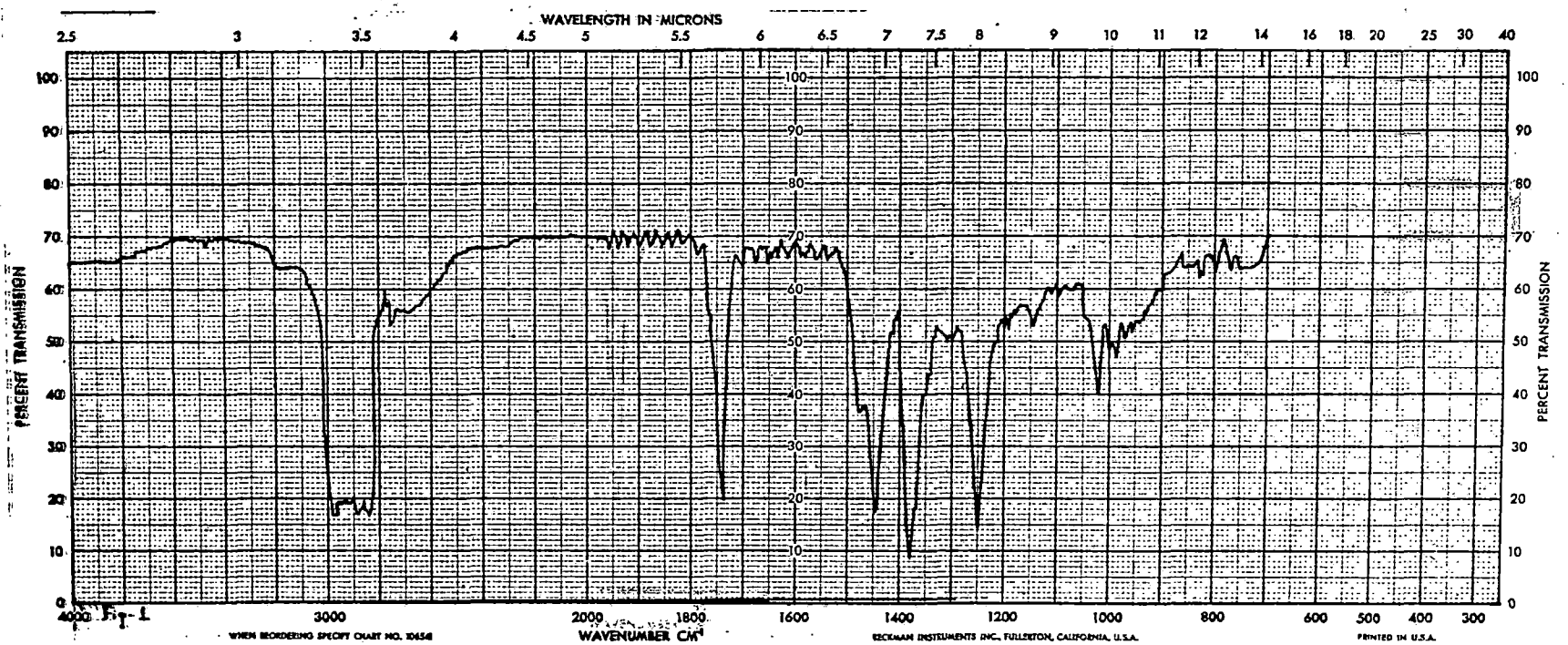


Fig-1

Fig.1: IR spectrum of 15-bromo-β-amyrin acetate 77.

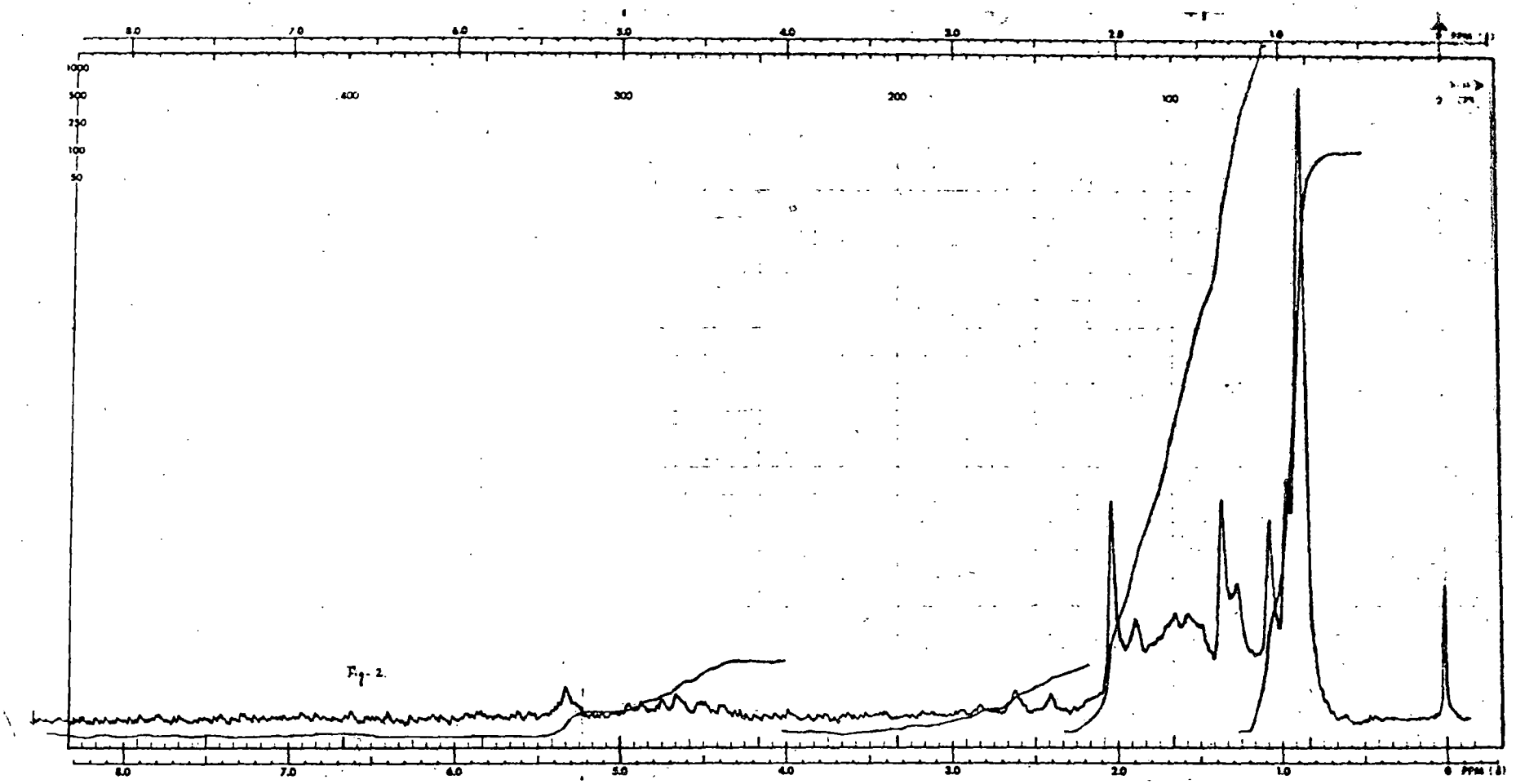
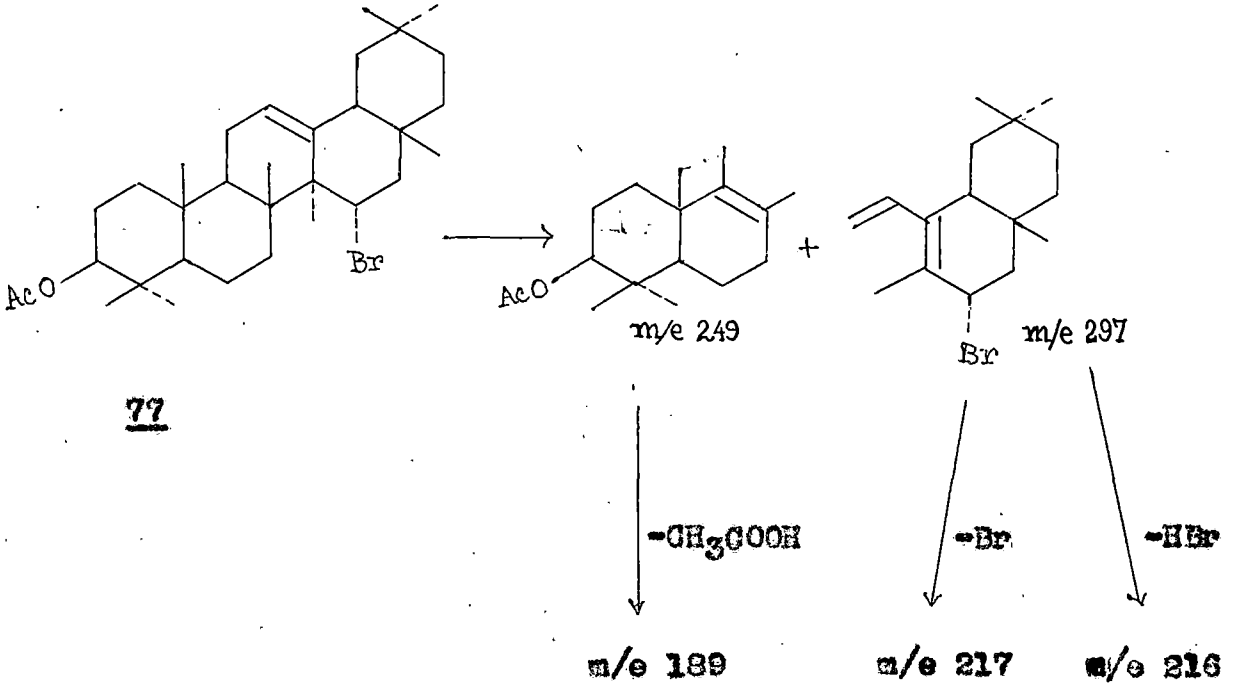


Fig.2: PMR spectrum of 15-bromo-β -amyrin acetate 77.

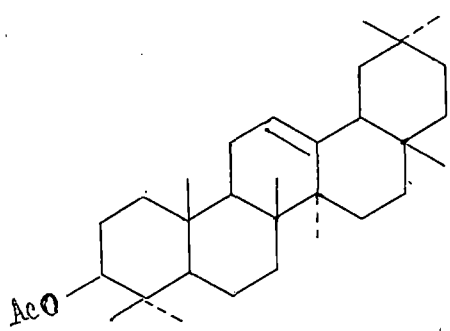
of 77 was finally confirmed by its mass fragmentation pattern. The compound showed a mass peak at m/e 548 (M^+) accompanied by other peaks at m/e 466 (M^+—HBr), 488 (M^+—AcOH), 406 (466—AcOH), 297, 249, 217, 216, 189. The fragmentation pattern may be explained if the double bond is assumed to be present at 12—13 position. The fragments at m/e 249 and 297 may be formed by Retro-Diels-Alder cleavage[43] of 12—13 double bond of structure 77 for the bromo compound. The genesis can be shown in Scheme—10:

Scheme—10

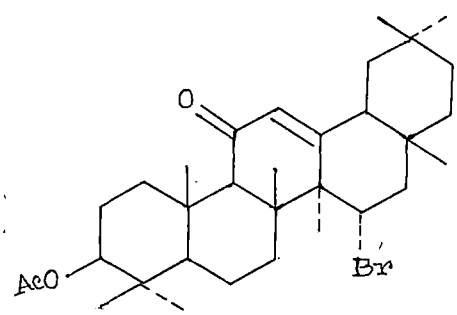


77

The structure of the compound as 77 was further established by the reaction with Zn dust in acetic acid on the compound that produced β-amyrin acetate 78, m.p. 230—31° (identical with an authentic specimen of β-amyrin acetate by mmp comparison).



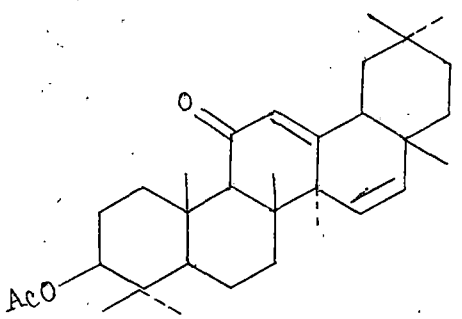
78



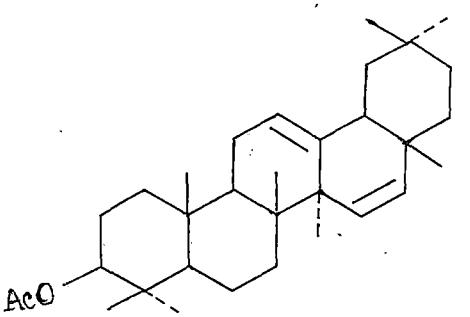
79

Oxidation of the bromo compound 77 with sodium-dichromate in presence of acetic acid furnished a gummy solid. Crystallisation of the compound from chloroform-methanol yielded 79, $C_{32}H_{49}O_3Br$, m.p. 240—41°, $[\alpha]_D$ +88°. UV absorption was found to be at the region λ max 249 nm and IR spectrum revealed that the compound had absorption at 1725, 1250 cm^{-1} (acetate) and 1680 cm^{-1} (—C=C—C=O). UV and IR spectrum confirmed the presence of an $\alpha\beta$-unsaturated carbonyl group. The compound was identified as 11-oxo-15-bromo-β-amyrenyl acetate[44] 79, when compared with an authentic specimen (mmp comparison) prepared by Khastgir and coworkers[44] from tarexeryl acetate.

Various attempts were made for dehydrobromination of the bromo ketone 79, to introduce the C—15—16 double bond. First it was tried by refluxing the compound with distilled dimethylaniline. In this case it was found that no dehydrobromination occurred and complete recovery of the starting material was obtained. As the dehydrobromination reaction was found to be not feasible by this reagent attempt was also made with s-collidine. The compound was refluxed with s-collidine for several hours and it was found that no reaction had taken place. Since the dehydrobromination could not be done even under forceful conditions it was assumed that probably some steric factors resisted dehydrobromination. As no dehydrobromination could be effected



80



81

for the preparation of 80, a reverse route was followed. First the bromo compound 77 was dehydrobrominated and then it was oxidised to produce 80.

The bromo compound 77 was refluxed with dimethyl-aniline for a period of six hours when usual work up afforded a solid which on crystallisation from chloroform-methanol gave a product, $C_{32}H_{50}O_2$, m.p. 199—200°, $[\alpha]_D$ +42°. No UV absorption was observed for the compound in the region 220—350 nm. Beilstein test for halogen was found to be negative. IR spectrum (Fig.3) of the compound showed the presence of an acetate group at 1730 and 1240 cm^{-1}. Peaks at 750 cm^{-1} ($\overset{H}{\underset{H}{>C=C<}}$) and 820 cm^{-1} ($>C=C\overset{H}{<}$) was also observed. PMR spectrum (Fig.4) of the compound 81 showed multiplet peak in the region 5.2 to 5.6 ppm for three hydrogens of vinyl groups. At 4.5 ppm the multiplet for one hydrogen of H—C—O—$COCH_3$ was observed. One singlet at 2.08 ppm for three hydrogens of —O—CO—CH_3 was obtained. At the region 0.8—1.2 ppm peaks were observed for eight tertiary methyl groups. From the IR and NMR spectra the structure of the diene was assigned as 81.

To prepare 11-keto compound of 3β-acetoxy-olean-12,15-diene, the compound 81 was oxidised by sodium dichromate in acetic acid in refluxing condition for a period of twenty four hours. After usual work up followed by crystallisation afforded a compound in about 80% yield, identified as 3β-acetoxy-11-oxo-olean-12,15-diene 80, $C_{32}H_{48}O_3$,

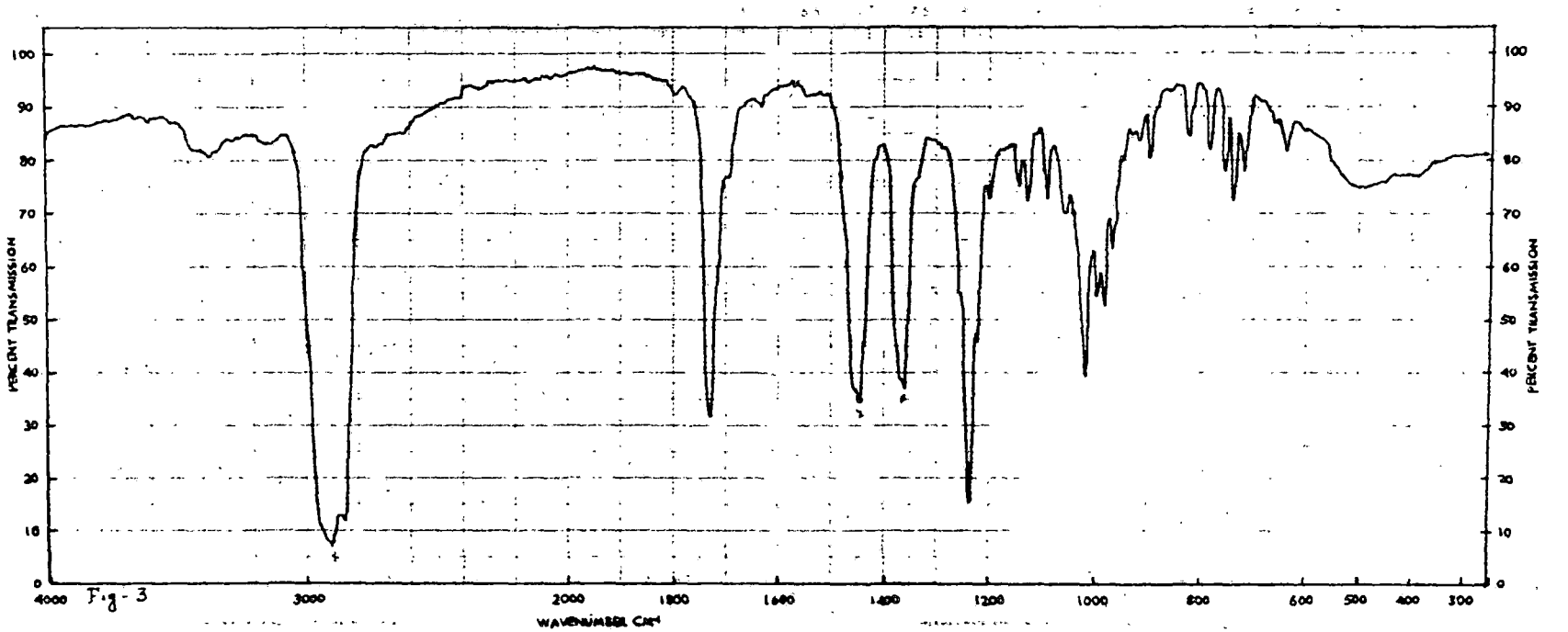


Fig.3: IR spectrum of olean-12,15-dien-3β-yl-acetate, 81.

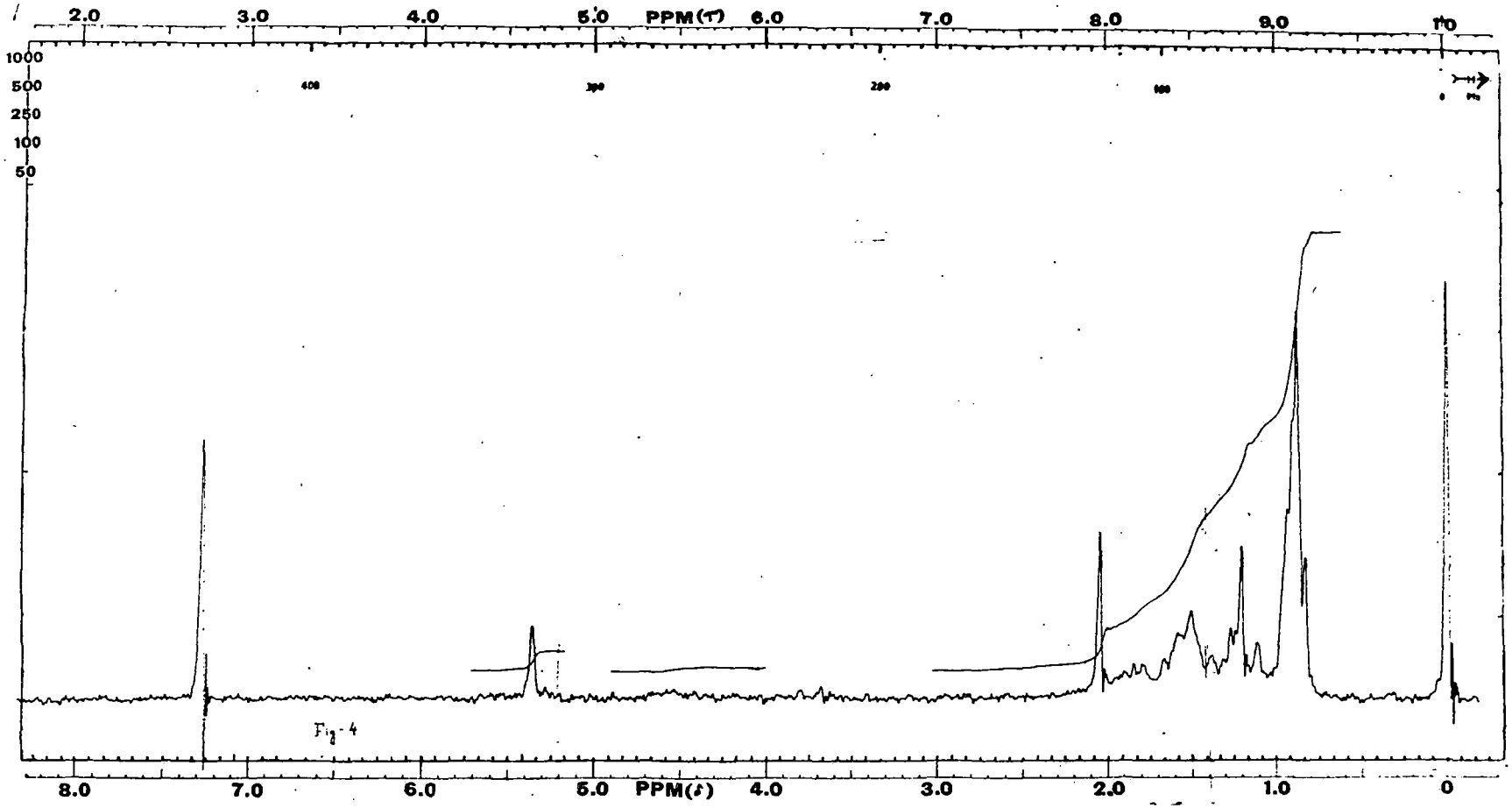
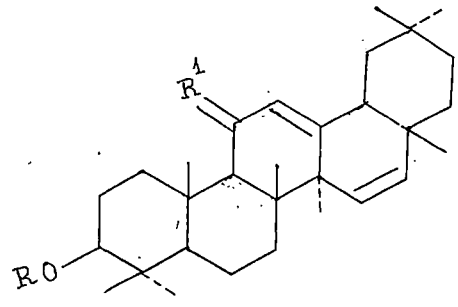
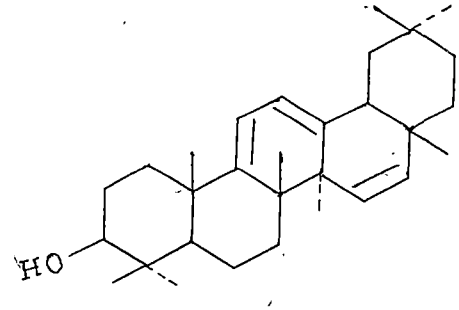


Fig.4: PMR spectrum of olean-12,15 dien-3β -yl-acetate, 81.

m.p. 243—45°, $[\alpha]_D$ +28.6°. UV absorption of the compound showed a maxima at λ_{max} 244 nm (ϵ = 11,376), which indicated the presence of an $\alpha\beta$-unsaturated ketone. IR spectrum (Fig.5) of the compound showed the presence of an acetoxy group at 1730 and 1240 cm^{-1}. The peak at 1660 cm^{-1} revealed that the compound contained an $\alpha\beta$-unsaturated ketonic functional group. Other peaks observed at 890 cm^{-1} and 750 cm^{-1} were due to the presence of —CH=CH— function. PMR spectrum (Fig.6) of the compound showed signals at 0.8 to 1.5 ppm for eight tertiary methyl groups present in the molecule. The acetoxy methyl protons appeared at 2.04 ppm. A multiplet was observed centred at 4.45 ppm for one proton of $\underline{H}—C—O—\overset{\overset{O}{\|}}{C}—CH_3$. Between 5.5—5.7 ppm peaks were obtained for three vinyl protons present in the molecule. On the basis of the above mentioned physical data the structure of the ketodiene could be assigned as 80.



80, R=AC; R^1=O
70, R=H ; R^1= 



82

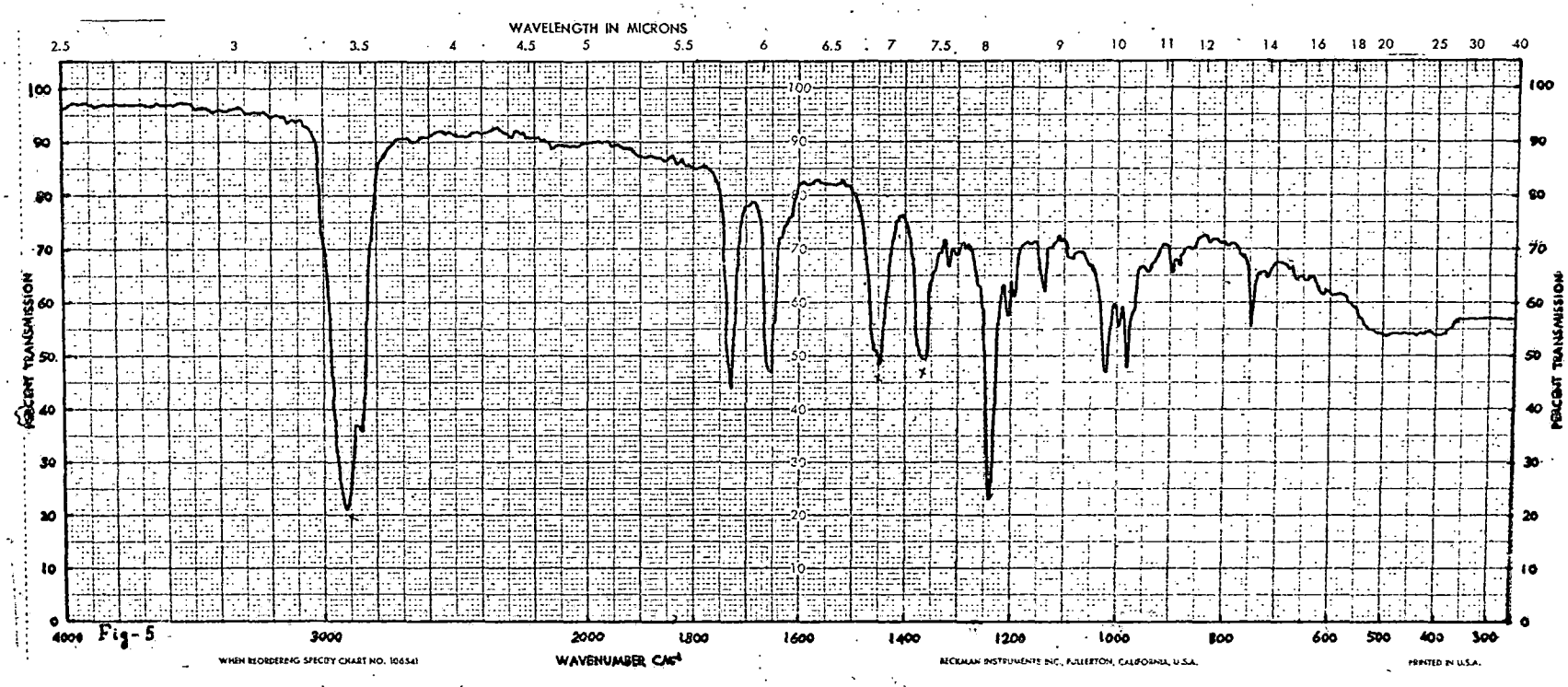


Fig.5: 3β -acetoxy-11-oxo-olean-12,15-diene, 80.

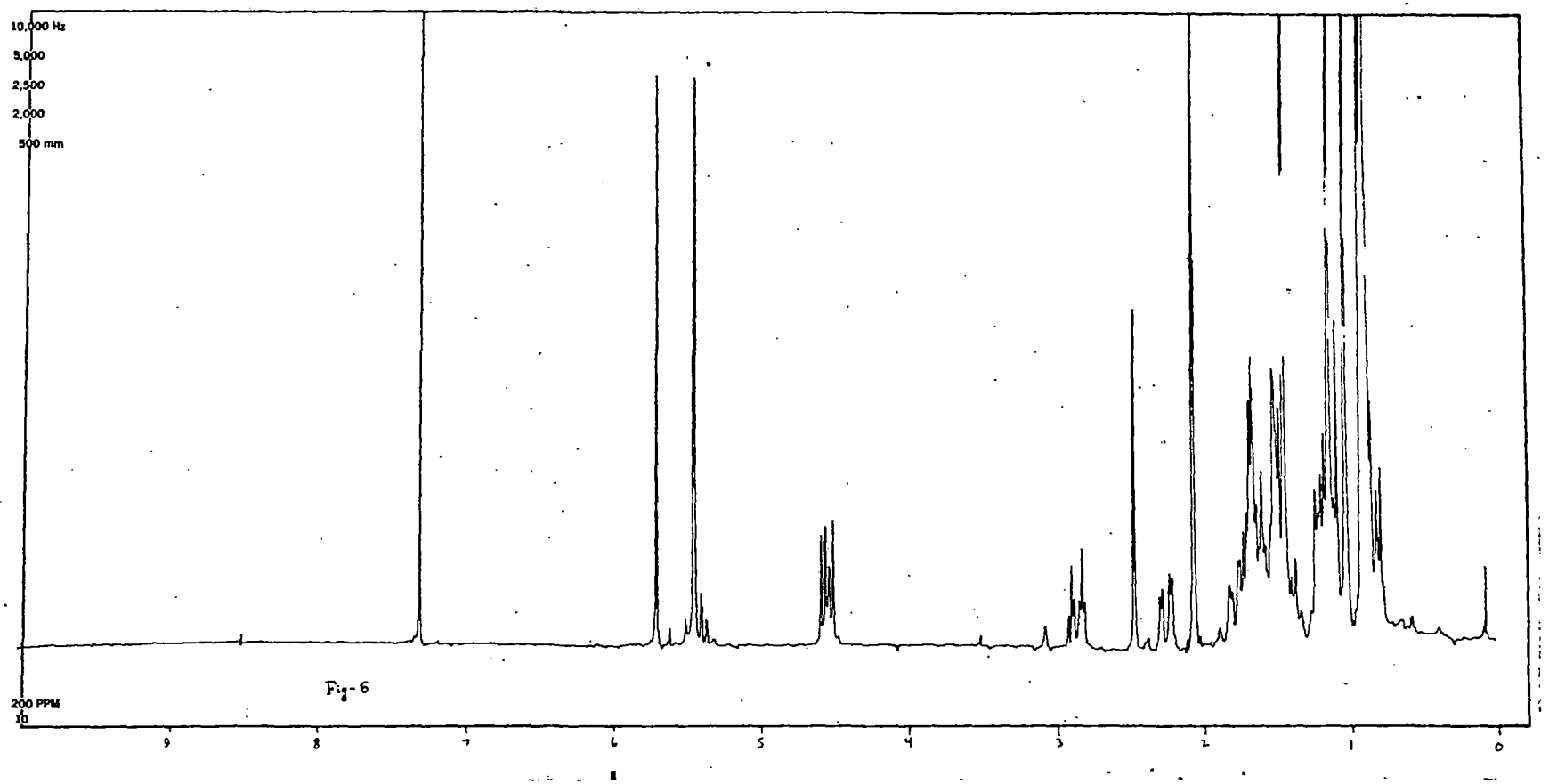
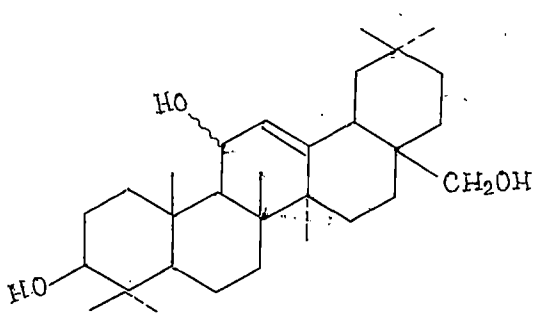
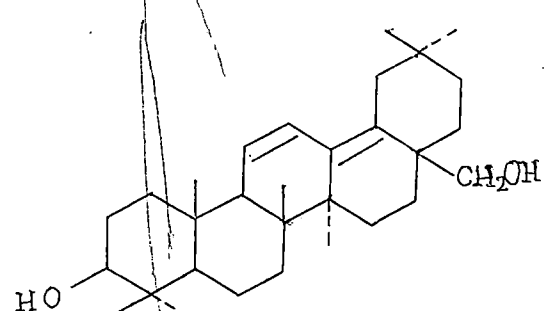


Fig.6: PMR spectrum of 3β -acetoxy-11-oxo-olean-12,15-diene, 60.

The ketodiene 80 was reduced by lithium aluminium hydride under refluxing condition for a period of six hours. The mixture was stirred at room temperature for 12 hours more. After usual work up the compound, $C_{30}H_{50}O_2$ 70, m.p. 198—200° was obtained. IR spectrum (Fig.7) of the compound showed ν max at 3460 cm^{-1} for —OH group and at 875 cm^{-1} for —CH=CH— function. It was found that if the compound was purified through column chromatography the newly introduced 11-hydroxy group underwent dehydration to form the homoannuler triene 82. The triene, $C_{30}H_{46}O_2$, m.p. 189—90° had the UV absorption at λ_{max} 276 nm (ϵ, 5260), indicating the presence of homoannuler diene system in ring C. This type of dehydration was reported earlier by I.Yosioka and coworkers[40], when 83 was heated producing the heteroannuler diene 84 (UV absorption at λ_{max} 244, 253, 263 nm).



83



84

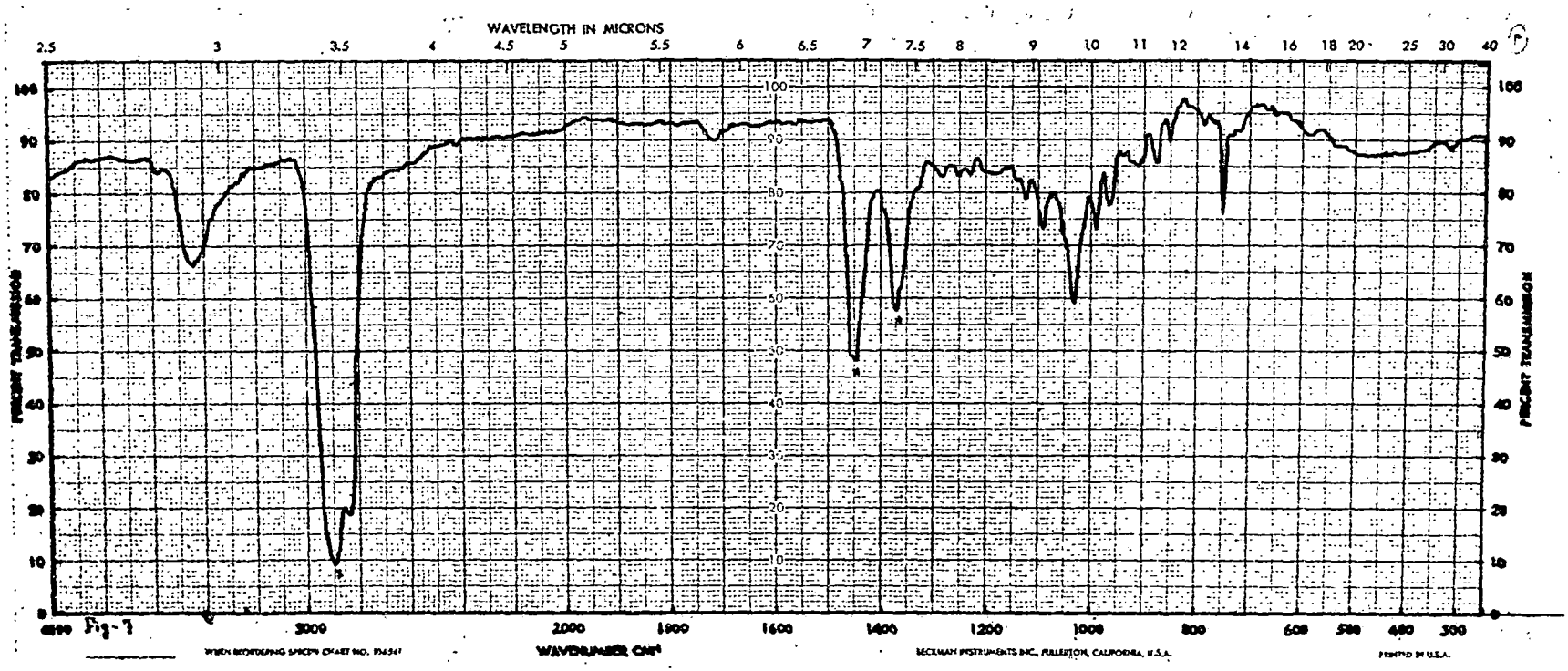


Fig-7

Fig.7: IR spectrum of olean-12,15-dien-3,11-diol, 70.

Formation of homoannuler diene in our compound is assumed for the fact, the heteroannular diene could not be produced due to the presence of a C—15,16 double bond.

So we had got the desired product 70, i.e. olean-12,15-dien-3,11-diol on which we could carry out the hydrogen peroxide reaction to get the desired products which we assumed before. The diol 70, was stirred at room temperature with a mixture of para toluene sulfonic acid, hydrogen peroxide and tertiary butyl alcohol following the procedure adopted by Covey and coworkers[23]. After stirring at room temperature for twenty four hours and usual work up the residue was chromatographed. A mixture of two compounds was eluted by benzene, TLC of which showed two distinct spots at very close range. The mixture of the two compounds were separated by fractional crystallisation. After crystallising several times the less soluble compound 85, $C_{30}H_{46}O_3$, m.p. 240—41° was obtained. No UV absorption was observed for the compound. IR spectrum (Fig.8) of the compound showed absorption in the region 890 and 820 cm^{-1} indicating the presence of HC═CH function, a peak at 3520 cm^{-1} for the hydroxyl group and another peak at 1775 cm^{-1} indicated that the compound contained a γ-lactone which was not

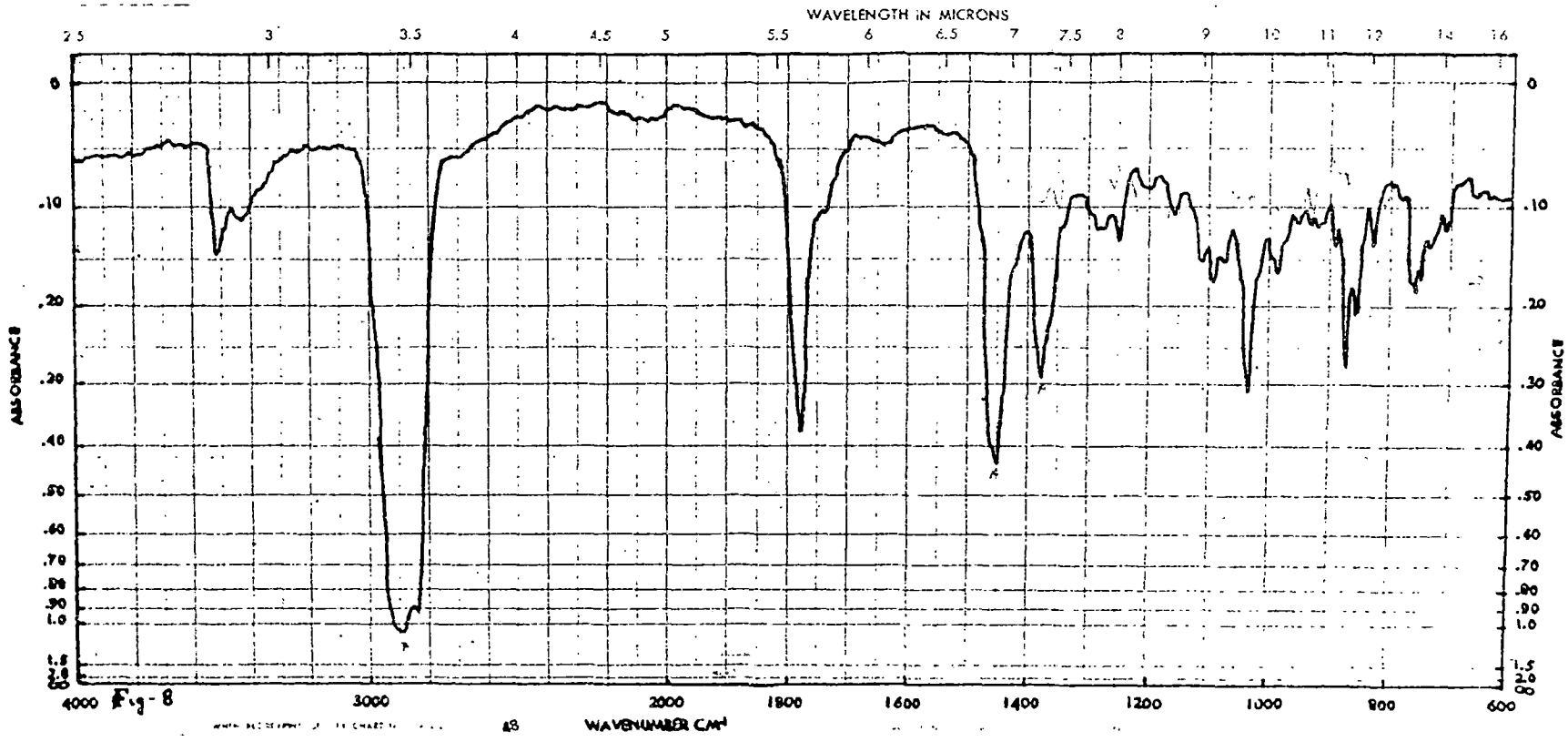
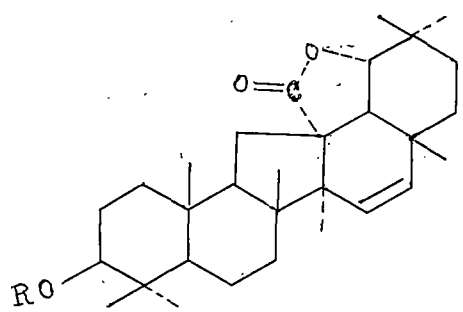


Fig.8: IR spectrum of the first hydroxy lactone (H_2O_2 oxidation product),85.

originally present in the starting alcohol. The compound 85, was acetylated at room temperature with acetic anhydride and pyridine.



85, R = H
85a, R = $COCH_3$

The acetate so formed was crystallised and after crystallisation gave a compound 85a, $C_{32}H_{48}O_4$, m.p. 215—16°. IR spectrum (Fig.9) of the compound 85a showed ν_{max} at 1780 cm^{-1} for γ-lactonic functional group. Peaks at 1720 and 1250 cm^{-1} indicated the presence of an acetoxy group. Other peaks at 890, 870, 750 cm^{-1} revealed that the compound contained a —C(H)=C(H)— double bond. The formation of a lactone had thus been proved by the IR spectrum of 85 and its acetate 85a. The structure of 85 has been conclusively established by its ^1H and ^{13}C NMR spectra and mass spectral analysis of its acetate 85a.

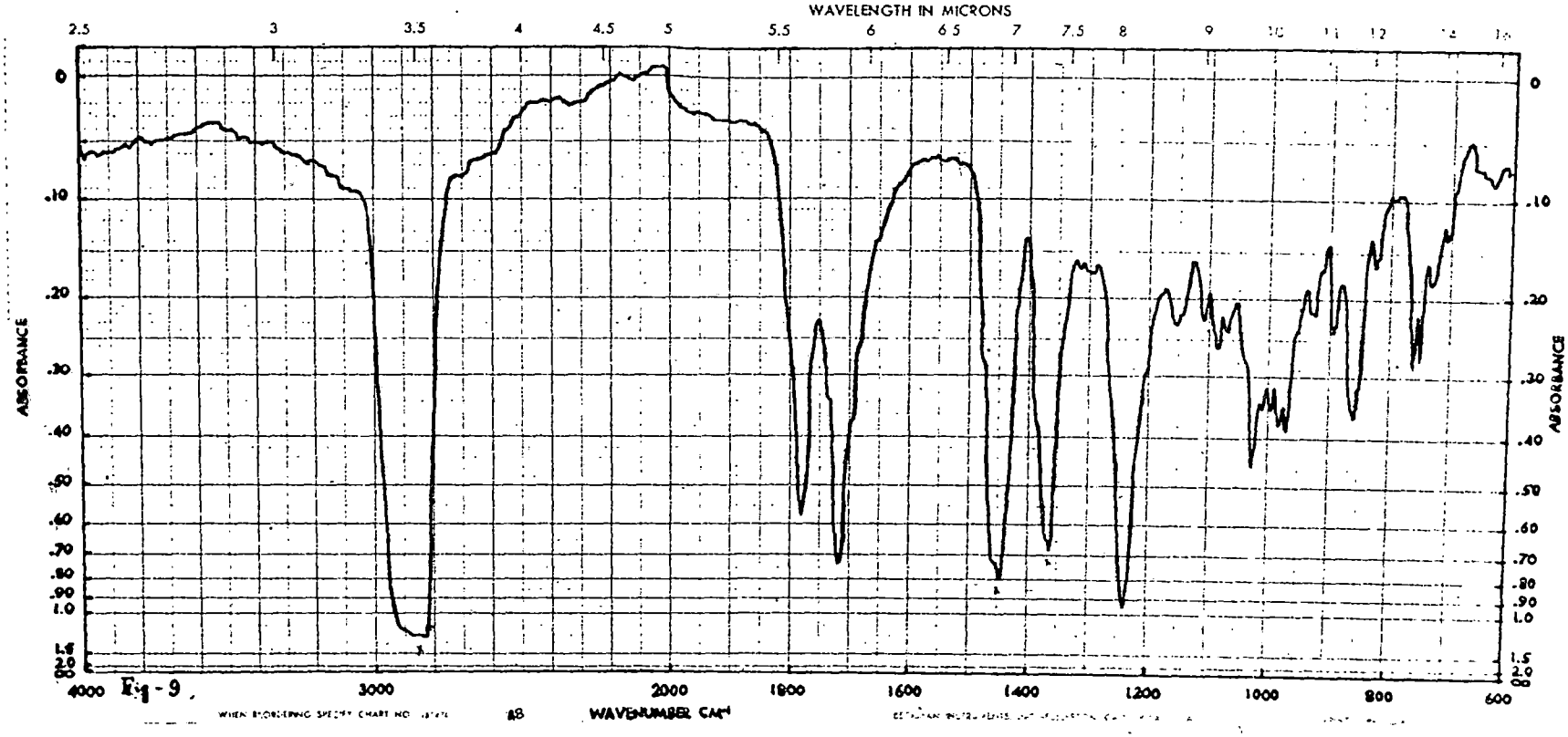


Fig-9

Fig.9: IR spectrum of the first lactone acetate, 85a.

^{1}H NMR spectrum (Fig.10) of the compound 85a showed the presence of eight tertiary methyl groups between 0.5 to 1.5 ppm. A singlet at 2.05 ppm indicated three protons of acetoxy methyl groups (—OCOCH_3). The doublet at 4.72 ppm (J=7.3 Hz) indicated the proton geminal to lactonic oxygen. The peak centred at 5.27 ppm, for cis disubstituted olefinic proton, was obtained as an AB quartet (J=10 Hz). Irradiation at 4.72 ppm (Fig.11) gave a singlet at 1.73 ppm showing the presence of a proton at 1.73 ppm to be coupled to the one at 4.72 ppm with J=7.5 Hz and weekly to other protons. Again irradiation at 1.73 ppm (Fig.12) at a fairly low level gave a sharp line at 4.72 ppm was due to the presence of a single proton adjacent to the lactonic oxygen that couples with a proton at 1.73 ppm. The multiplet at 4.5 ppm collapsed to a broard singlet (Fig.13) suggesting the proton at C—8 coupled with the protons at C—2. The absence of any peaks between 2.2 and 3.5 ppm showed that the C—α to the lactonic —CO— possessed no proton. The above observation could be explained if the lactonic —CO— group was attached to the C—13 position and the γ-lactone ring was formed with the C—19 carbon with a geminal β-H that had a single neighbouring β-axial proton at C—13 position. Thus the ^{1}H NMR and IR spectra suggested structure 85, for the hydroxy and 85a, for the corresponding acetate.

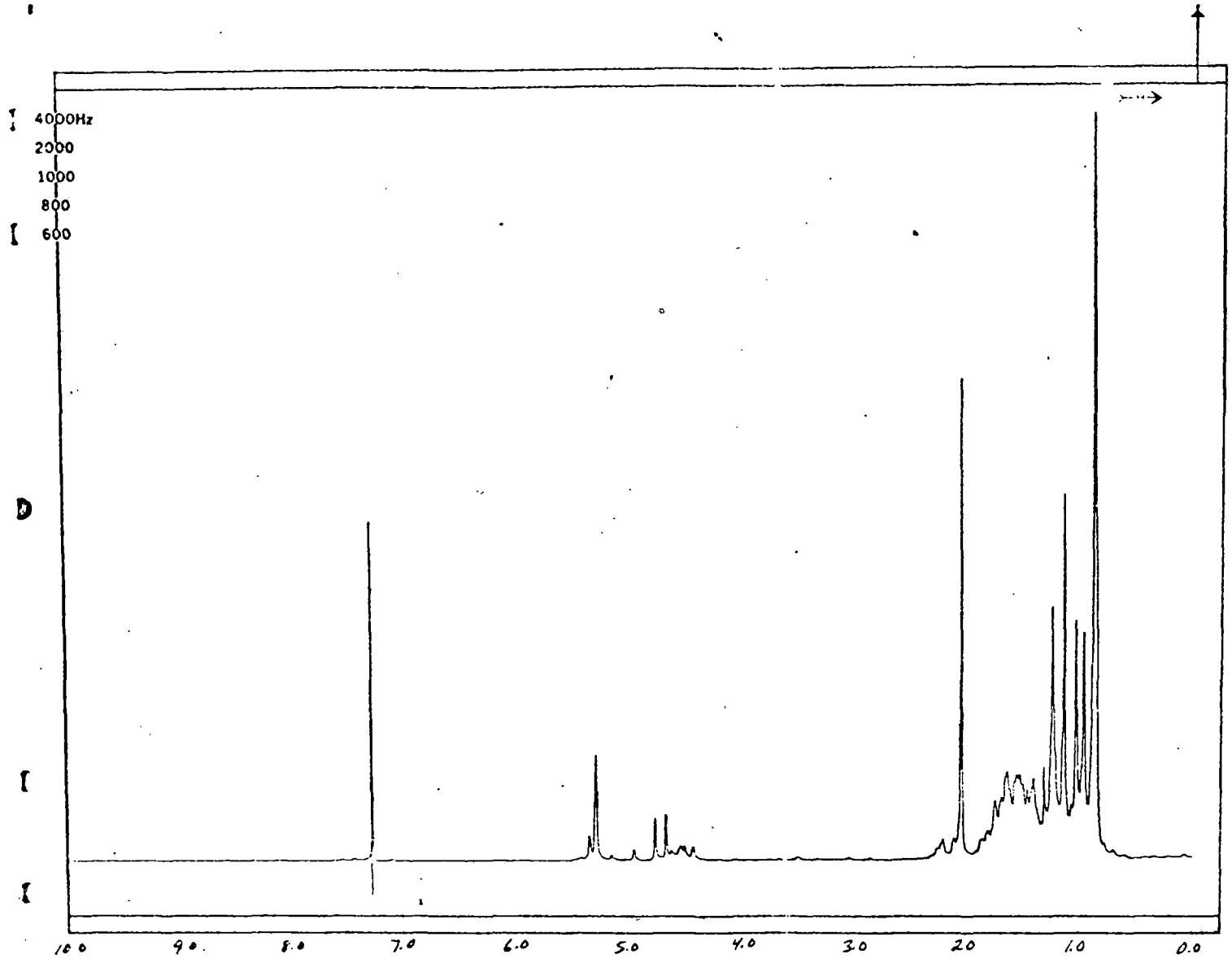


Fig.10: PMR spectrum of first lactone acetate, 85a.

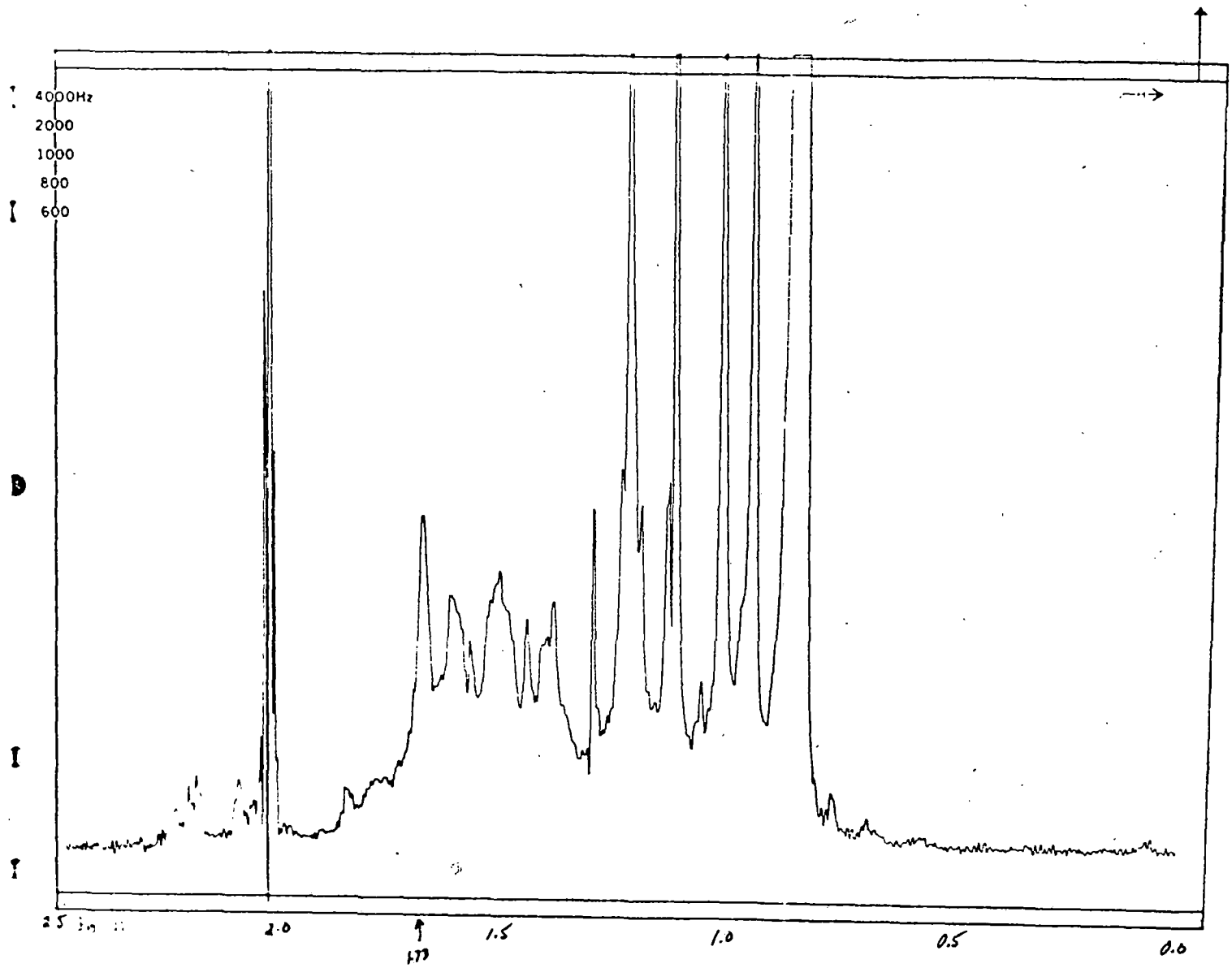


Fig.11: PMR spectrum of the first lactone acetate, 85a(irradiation at 4.72ppm)

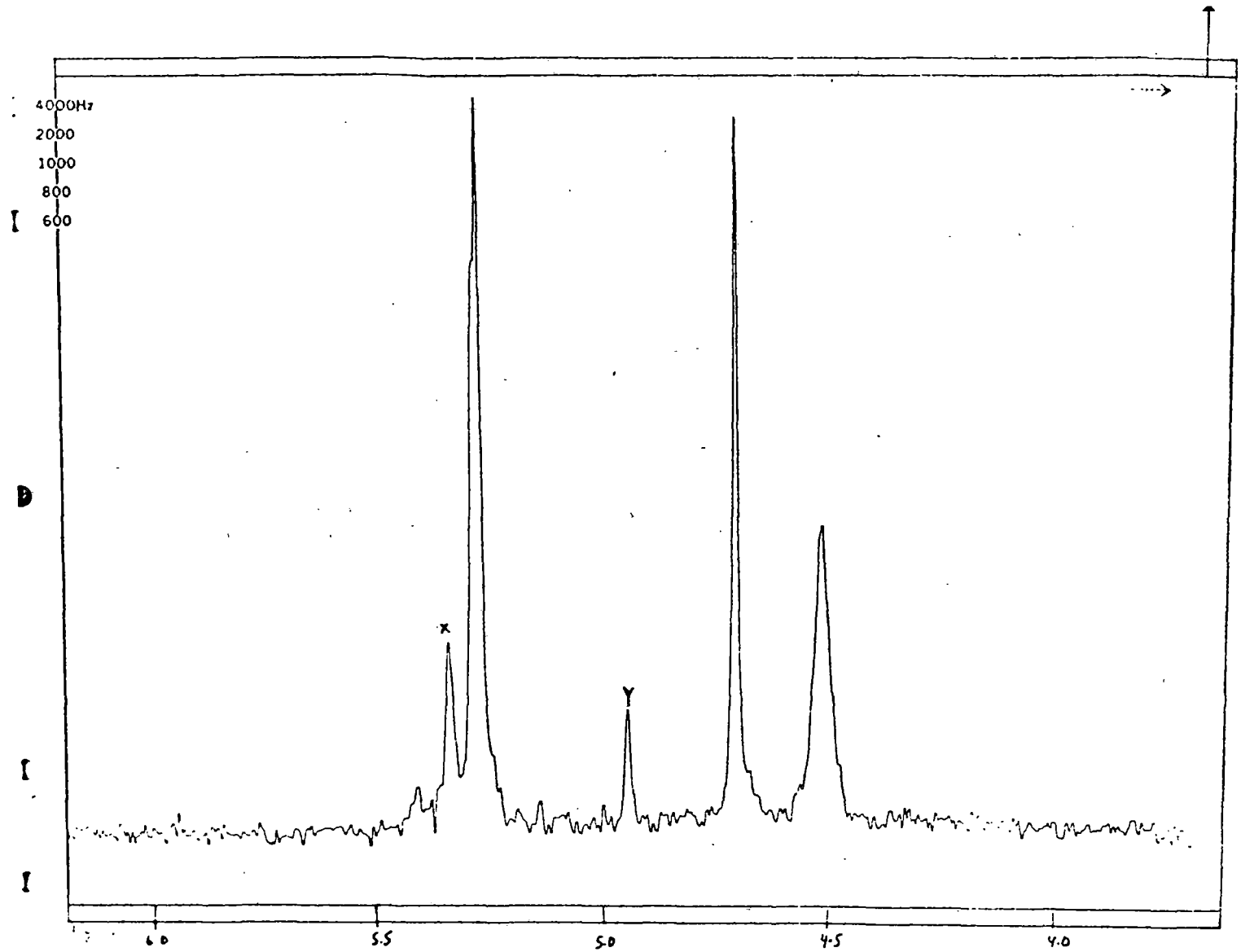


Fig.12: PMR spectrum of the first lactone acetate, 85a(irradiation at 1.73 ppm).

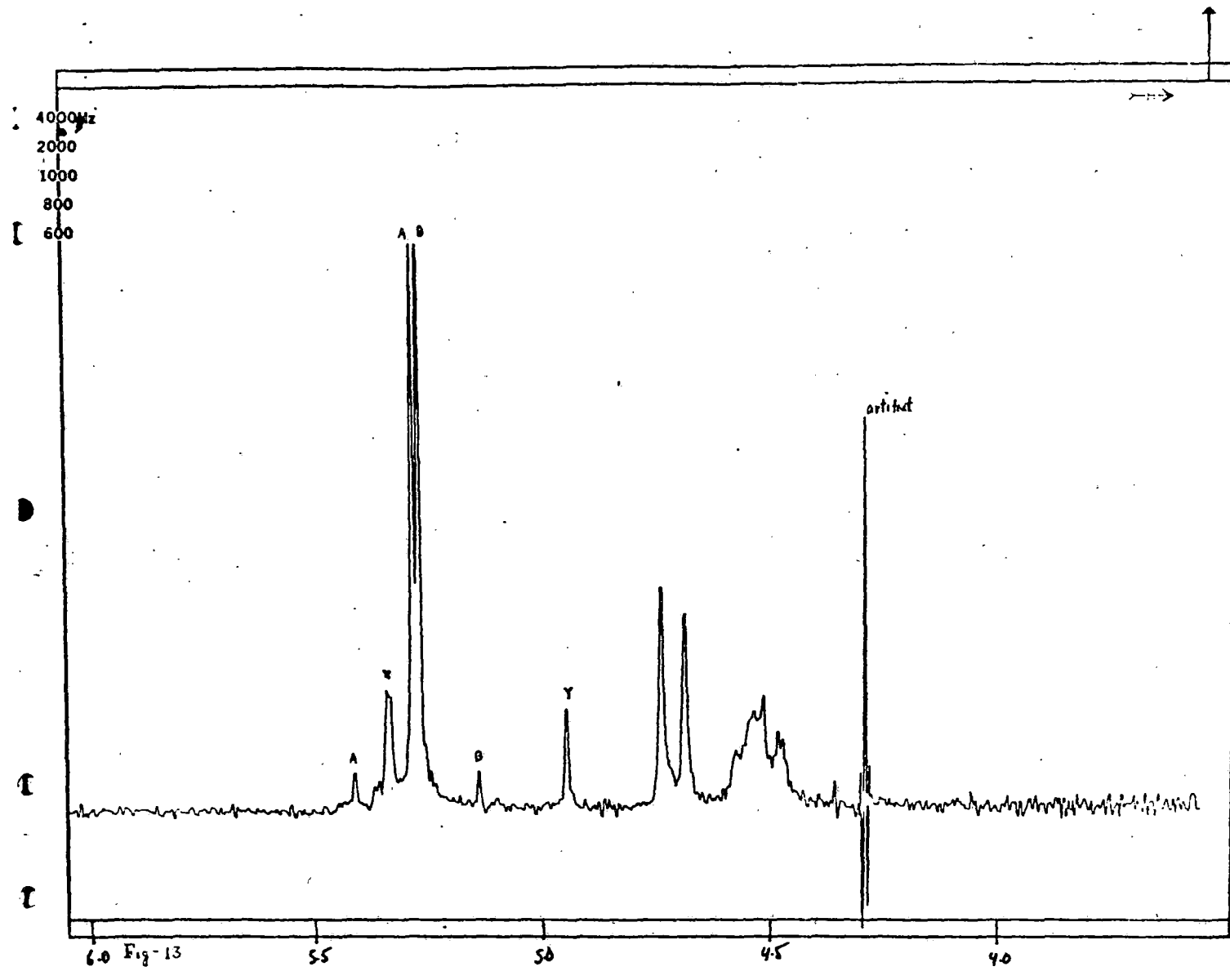
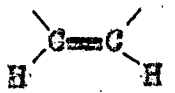


Fig.13: PMR spectrum of first lactone acetate, 85a (plot expansion).

The structure was corroborated by its ^{13}C NMR and mass spectral analysis.

^{13}C NMR spectrum (Fig.14) of the compound 85a showed that there were two singlets at 170.5 and 175.7 ppm which were due to the C—3 acetate, carbonyl and the lactonic carbonyl carbons respectively. The singlet at 175.7 ppm fairly indicated that it was either five or six membered ring lactone. The singlets at 80 and 82 ppm were doublets and were to be due to C—H groups bonded to oxygen of an ester. Thus one of the doublets was due to O—C—H group at C—3 position and the oxygen of the lactone must also contain at least one O—C—H group attached to it. The doublets at 132.75 and 130.6 ppm indicated that the double bond was counted as disubstituted olefinic bond i.e.  .

Mass spectrum (Fig.15) of the compound 85a showed the molecular ion peak at m/e 496. The other fragments obtained were at m/e 468 (M^+—CO), 452 (M^+—CO_2), 436 (M^+—AcOH), 421, 408, 392, 372, 313, 300, 269, 257, 244, 231, 217, 218, 208, 203, 191, 189, 187, 175, 171, 161, 147, 135.

Thus the first hydroxy lactone has been established as 3β-hydroxy-C-12-nor-olean-15-en-13α-carb-19α-olide 85.

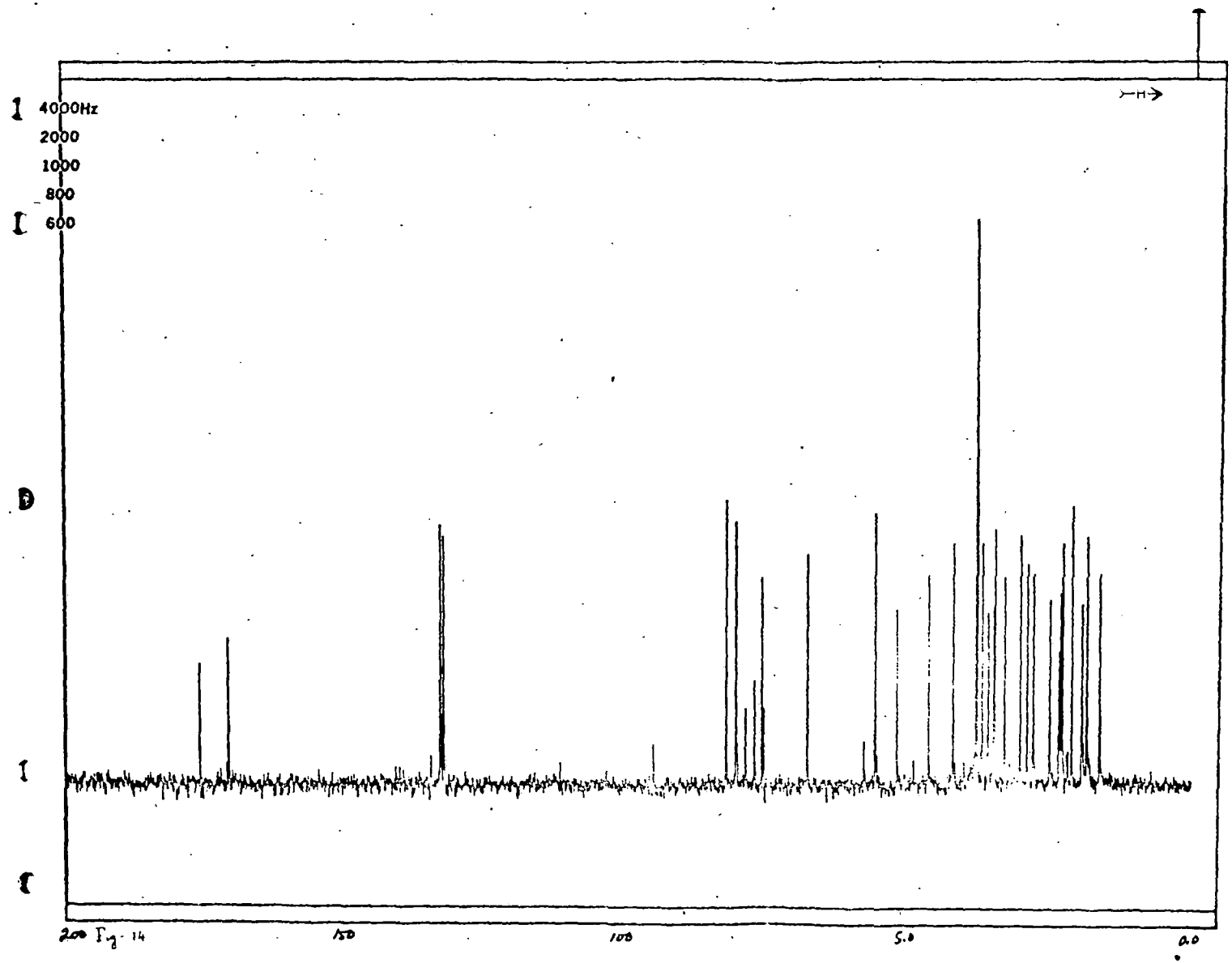


Fig.14: ^{13}C NMR spectrum of first lactone acetate, 85a.

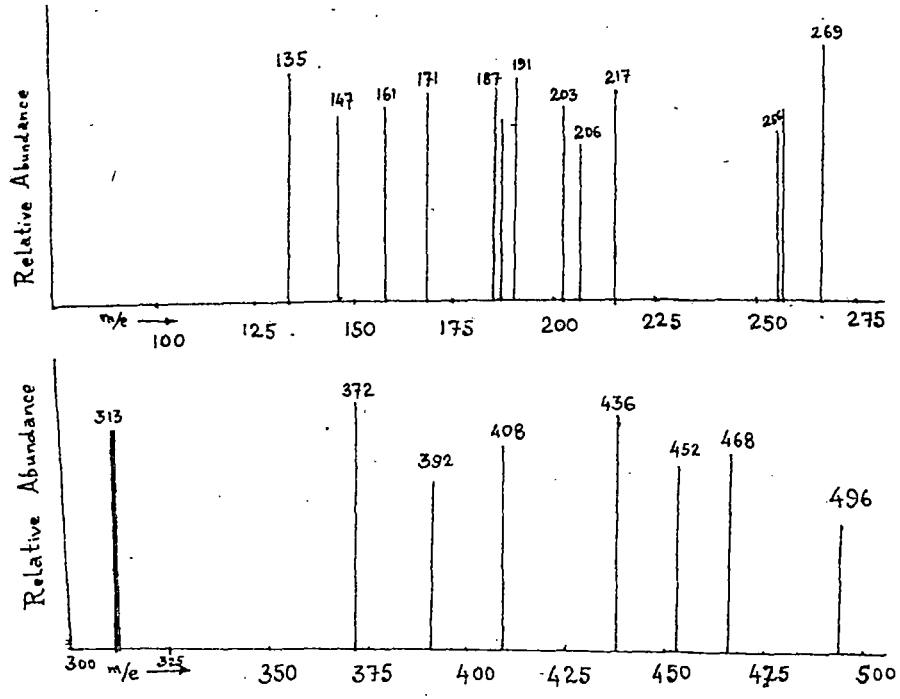


Fig 15 : Mass spectrum of the first lactone acetate, 85a.

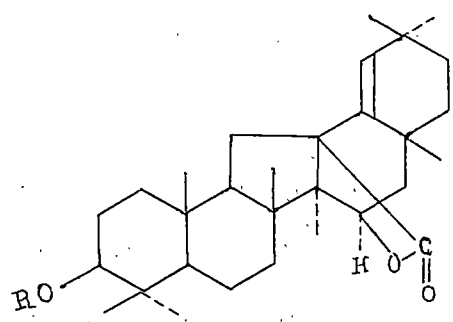
Isolation of the second compound 86:

The filtrate after repeated separation of the lactone 85, on concentration and crystallisation from chloroform-methanol mixture yielded another crystalline compound. The compound was purified by repeated crystallisation. After crystallization the compound 86, so obtained was analysed for molecular formula, $C_{30}H_{46}O_3$, m.p. 256—57°, no UV absorption was observed for the compound. IR spectrum of the compound showed peaks at 3520 cm^{-1} for hydroxyl functional group, 1780 cm^{-1} for a γ-lactone and 820 cm^{-1} for a trisubstituted double bond present in the molecule. The structure of the isomeric compound was proved by its IR, ^1H, ^{13}C NMR and mass spectral analysis of its acetate 86a, ^1H NMR spectrum of the compound 86, showed a singlet at 5.3 ppm for the vinyl proton. A multiplet at the region 4.9 ppm ($W_{\frac{1}{2}}$ = 20 Hz) was obtained due to the proton geminal to the lactonic oxygen which might have two neighbouring protons. A triplet at the region 3.23 ppm was obtained ($W_{\frac{1}{2}}$ = 20 Hz) for the proton geminal to the OH at C—3 present as an axial proton[45].

Mass spectrum of the compound 86, showed a molecular ion peak at m/e 454(M^+). Other fragments at m/e 436

(M^+-H_2O), 426 (M^+-CO), 410 (M^+-CO_2), 408, 392, 313, 269, 231, 205, 189, 187, 171 were obtained.

Acetylation of the compound 86 in presence of acetic anhydride and pyridine at room temperature was done and the product 86a, obtained after usual work up and crystallisation was analysed for $C_{32}H_{48}O_2$, m.p. 228—29°.



86, R = H
86a, R = CH_3CO

IR spectrum (Fig.16) of the compound 86a showed the presence of γ-lactone at 1780 cm^{-1} and peaks at 1730 and 1250 cm^{-1} were due to the acetate functional group present in the molecule. Another peak at 820 cm^{-1} was due to presence of a trisubstituted double bond.

^1H NMR spectrum of the compound 86a showed a multiplet at the region 4.8 ppm ($W_{\frac{1}{2}}$ = 7Hz) and found integrated

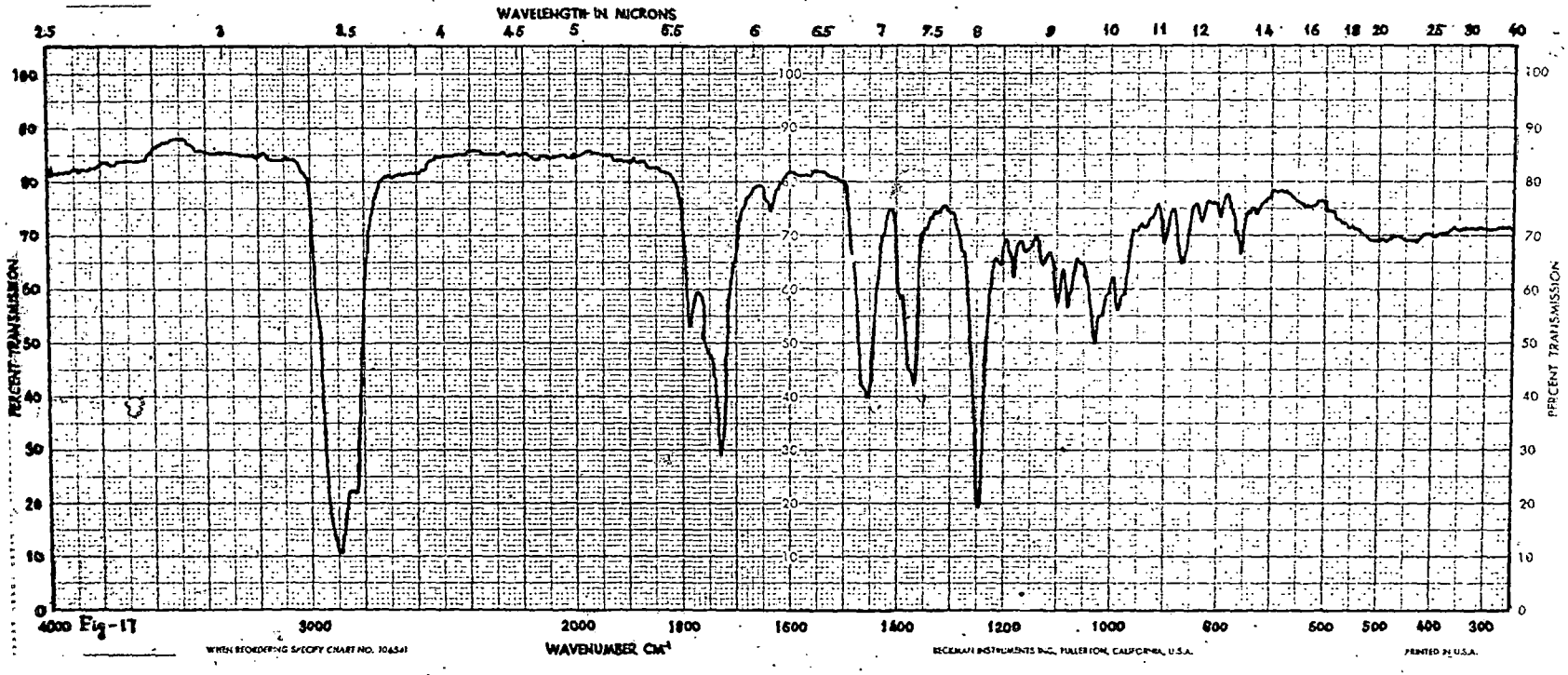
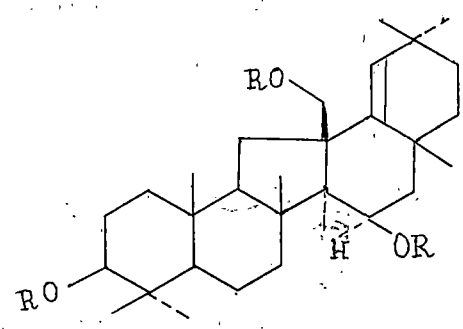


Fig.16: IR spectrum of secone lactone acetate, 86a.

for one proton was due to the fact that the proton geminal to the lactonic oxygen is equatorial which coupled with neighbouring axial and equatorial protons. The multiplet obtained in the region 4.5 ppm was due to C—3 proton. The singlet obtained at 5.3 ppm for a vinyl proton was possible only if the double bond is at C—18—19 position so that the proton at C—19 would give a singlet. The absence of any peak in the region 2.2 to 3.5 ppm showed that the lactonic —CO— had no α-H as in 85a and hence should be attached to the same carbon (C—13). The absence of A—B quartet for the cis C—15—16 olefinic protons present in 85a, indicated that this double bond must be involved in the formation of the lactone 86 and the lactyl oxygen should be attached to C—15 with an α-equatorial geminal proton that coupled with C—16 protons. The structure of 86, as well as 86a was thus proved. The mass spectrum of 86a was almost same as that of 85a.

The structure of the second lactone 86 was finally proved by the cleavage of the lactonic ring. Lithium aluminium hydride reduction of the lactone 86, yielded a solid which on crystallisation from chloroform and methanol afforded crystals of 87, that was analysed for $C_{30}H_{50}O_3$, m.p. 280—82°. The compound was found to be a triol, which

was proved by the IR, ^{1}H and ^{13}C NMR and mass spectral analysis of the acetylated product of triol i.e. 87a.



87, R = H
87a, R = CH_3CO

After acetylation of the triol 87, with acetic anhydride and pyridine at room temperature and crystallization of the product from chloroform and methanol, the acetate 87a, m.p. 190—93° was obtained. Elemental analysis showed it to be a triacetate having molecular formula $C_{36}H_{56}O_6$. IR spectrum (Fig.17) of the compound 87a, showed the broard peaks at ν_{max} 1735—40 cm^{-1} and 1250—1240 cm^{-1} that were due to the presence of acetate groups. Peak at 820 cm^{-1} showed that the compound contained a trisubstituted double bond. ^{1}H NMR spectrum (Fig.18) of the triacetate showed peaks in the region 0.88 to 1.2 ppm for eight tertiary

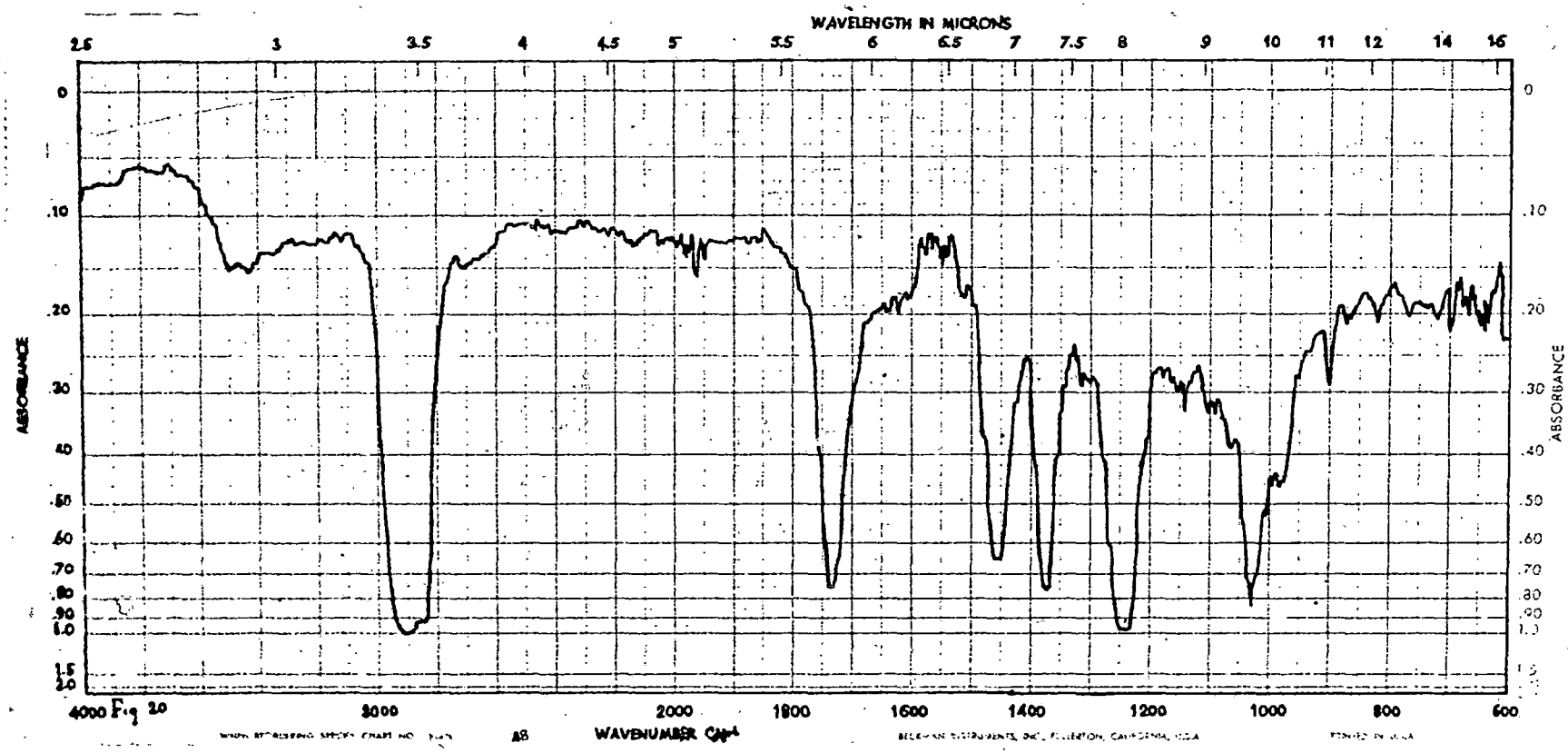


Fig.17: IR spectrum of the triacetate, 87a.

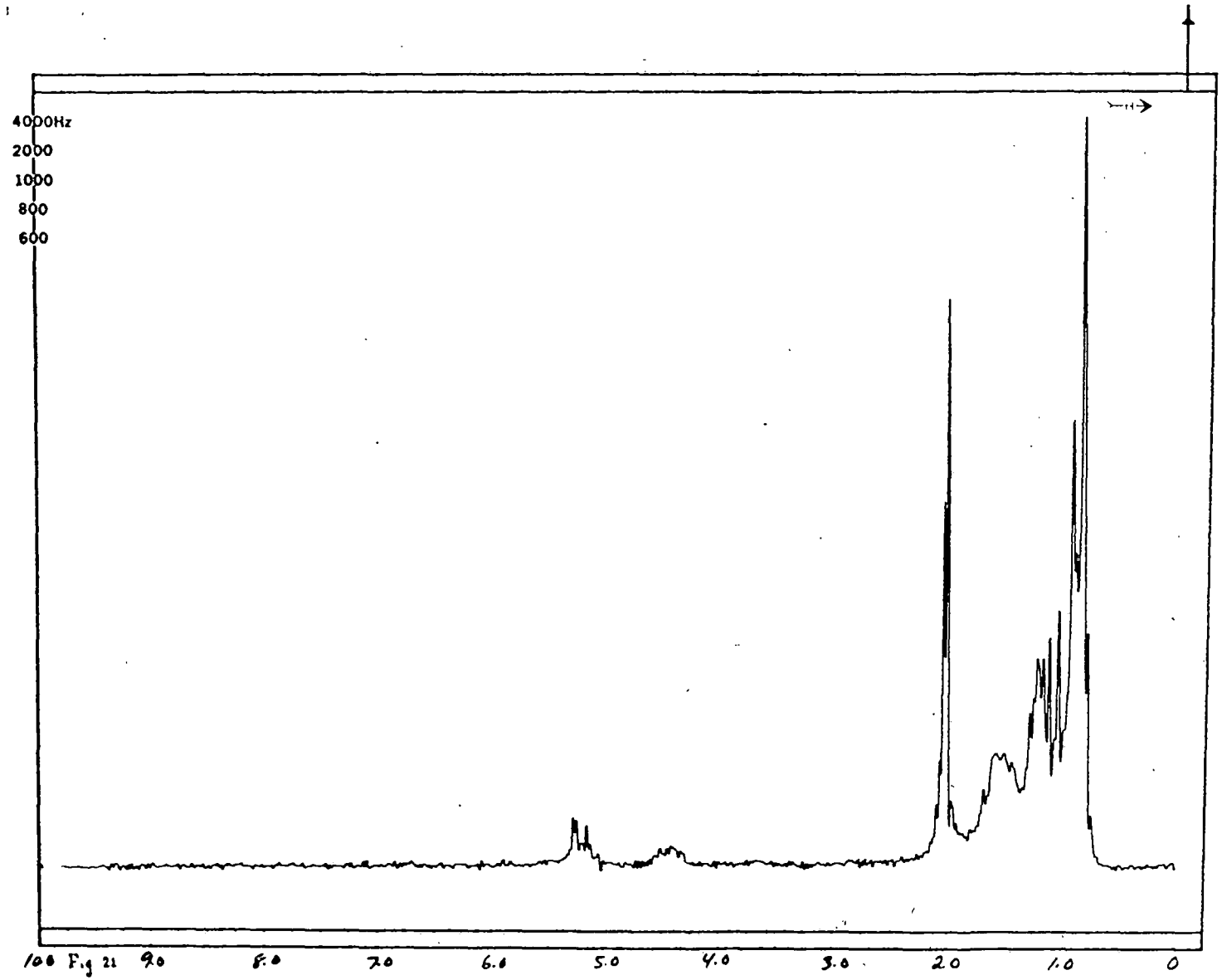


Fig.18: PMR spectrum of the triacetate, 87a.

methyl groups, the peak at the region 2.05 to 2.1 ppm showed the presence of three acetoxy methyl groups, the multiplet centred at 4.45 ppm was due to the proton at C—3 and two methylene groups geminal to acetate groups. At the region 5.3 ppm (J=8Hz), a doublet split into a multiplet might be due to the C—15 proton geminal to the acetate. The singlet at 5.3 ppm indicated the presence of a vinyl proton which had no neighbouring proton, such a vinyl proton is possible only if the double bond is situated at C—18—19 position of common pentacyclic triterpenoids. So the ^{1}H NMR spectrum of the triacetate suggested the structure as 87a. The structure of 87a was corroborated by its ^{13}C NMR and mass spectral analysis.

^{13}C NMR (Fig.19) of the compound 87a, showed that there were three singlets at 170.2 and 170 ppm which were due to three acetoxy carbonyl functions present in the molecule. The compound showed the doublets at 80.5 and 78.5 ppm due to the presence of —CH—O—CO—functional group in the molecule. The singlet at 155.5 and doublet at 122 ppm assured the presence of C=C$\diagup\!\!\diagdown_{H}$ double bond. Mass spectrum (Fig.20) of the triacetate 87a, showed a molecular ion peak (M^{+}) at m/e 584, the other prominent peaks were obtained at m/e 524

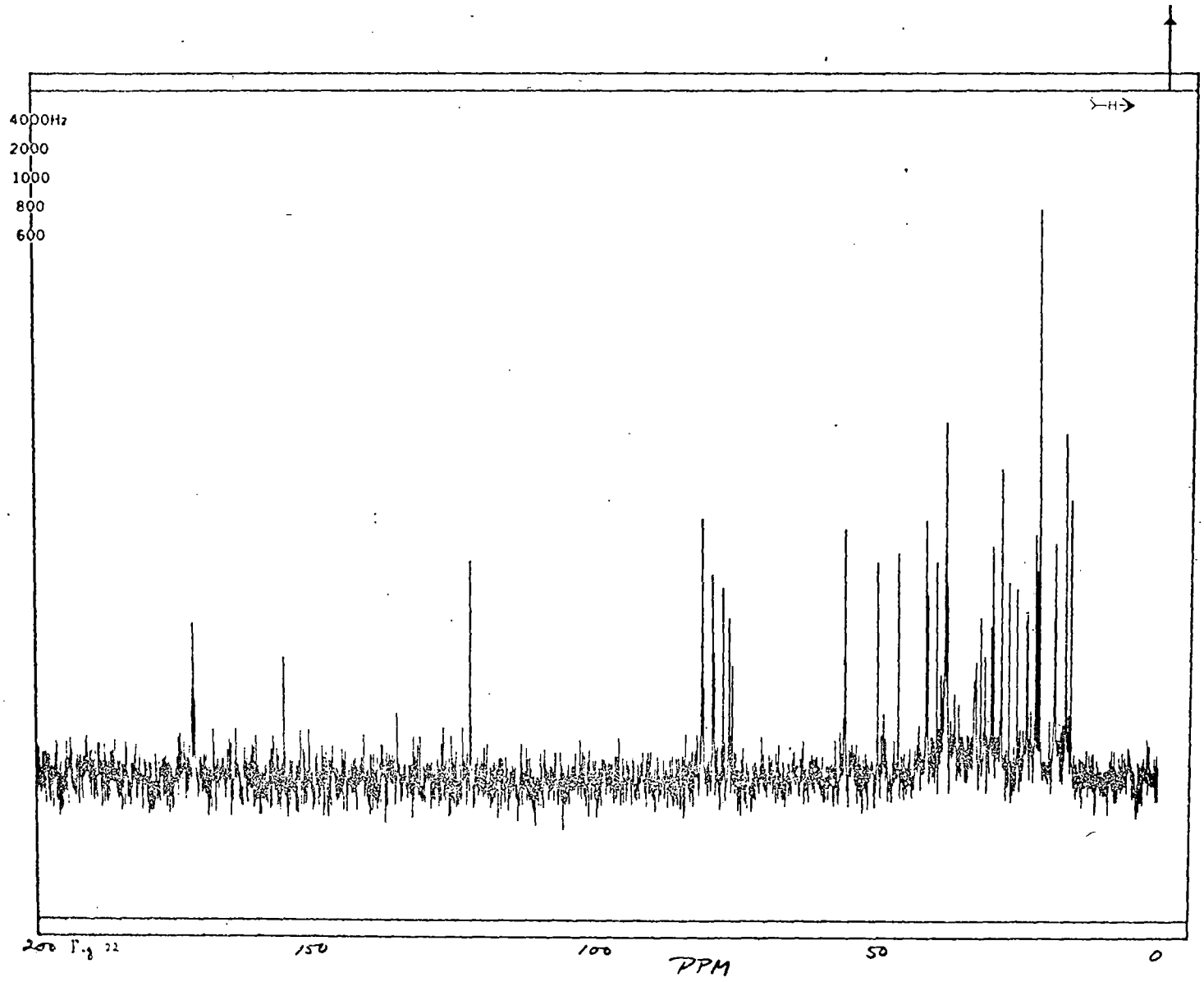


Fig.19: ^{13}C NMR spectrum of the triacetate, 87a.

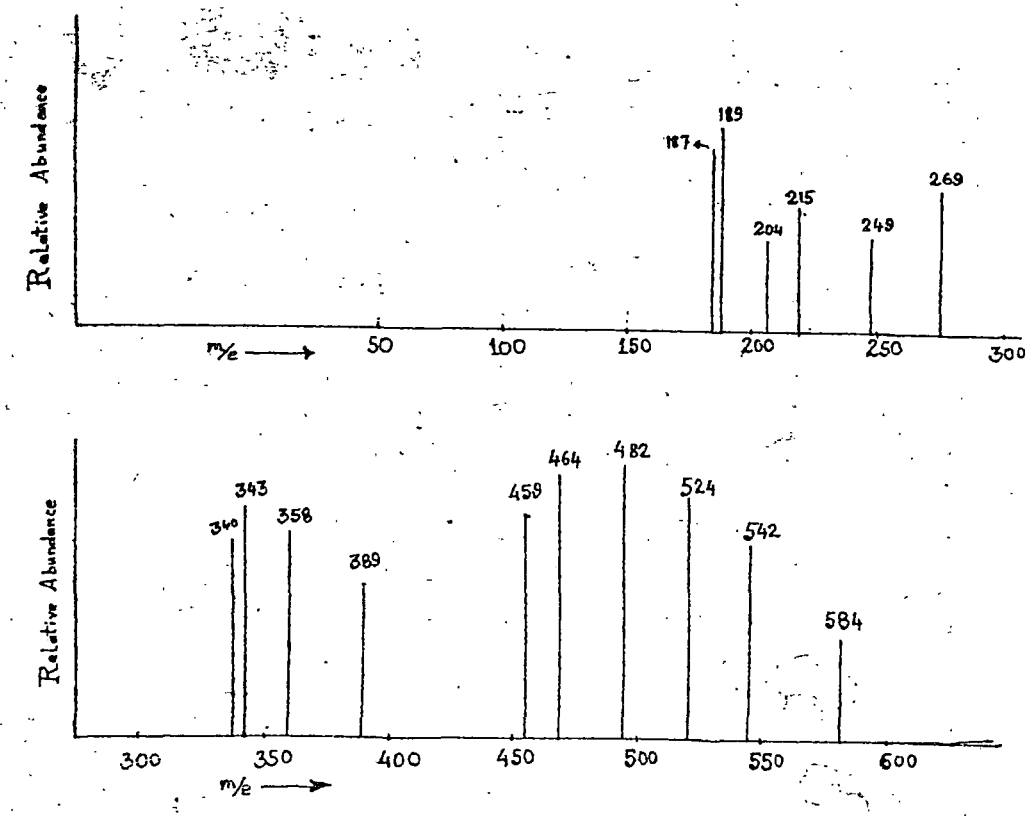


Fig 20 : Mass spectrum of the triacetate, 87a.

(M^+—ACOH), 432, 464 (M^+—2ACOH), 459, 389, 358, 343, 340, 269, 249, 215, 204, 188, 187.

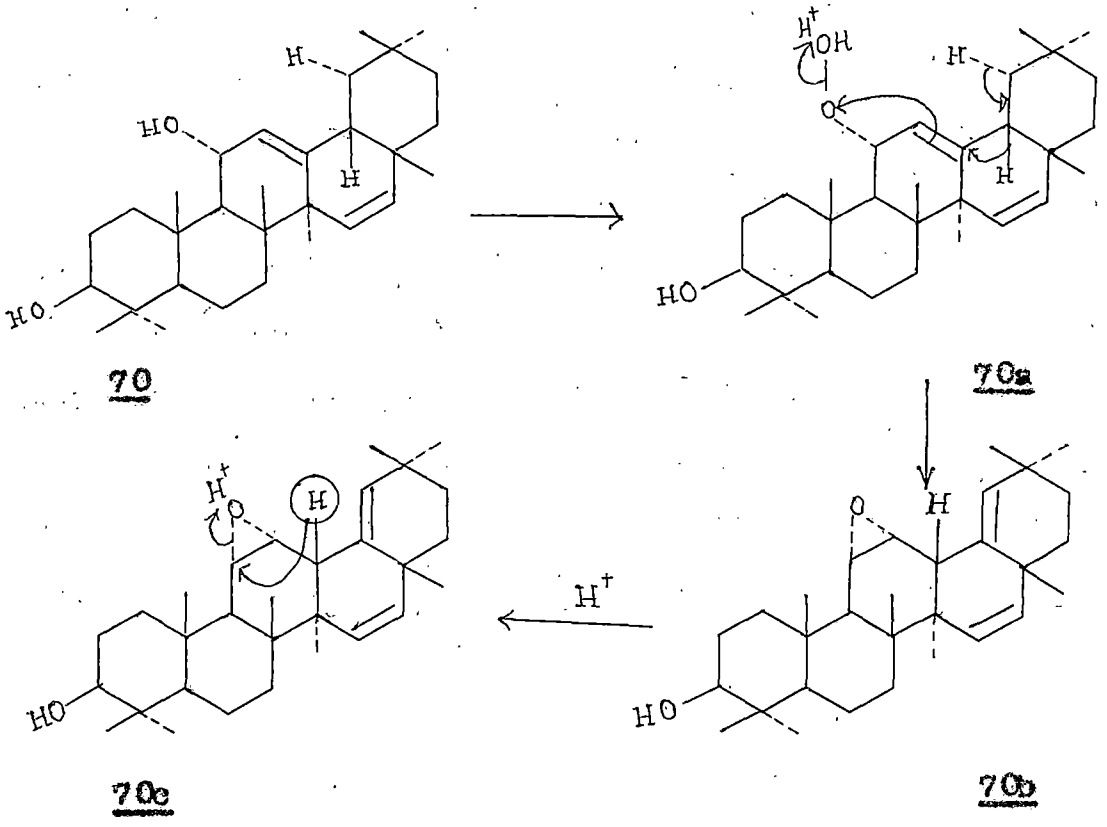
Hence from the above physical data the structure of the triacetate has been assigned as C—12-nor-olean-18-19-en-3β, 12, 15β-triacetate. This confirmed the structure of the second lactone as 86, lithium aluminium hydride reduction and acetylation of which furnished the triacetate 87a.

Mechanism of the formation of two lactones 85 and 86:

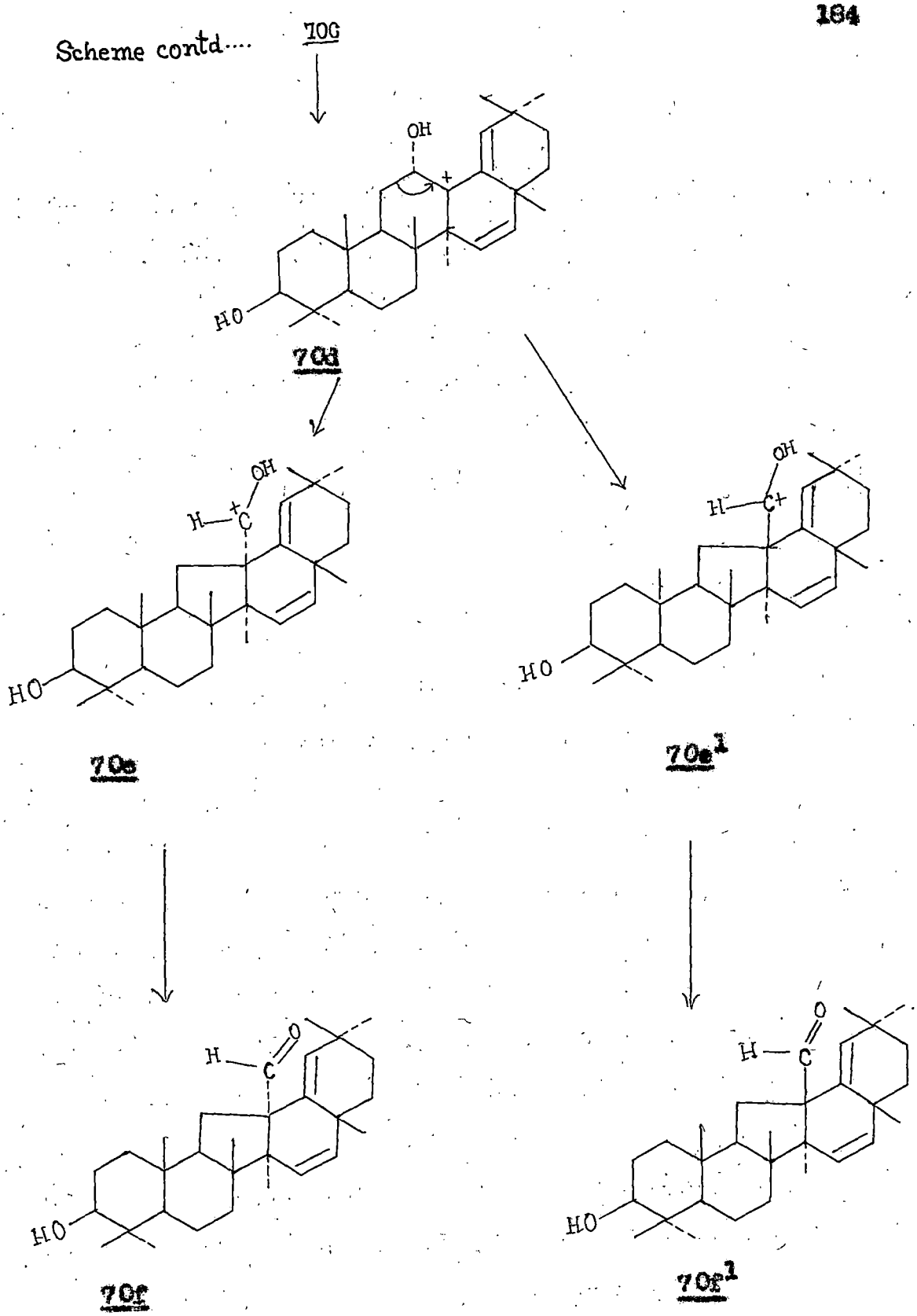
The intermediates formed in the mechanism of formation of two lactones 85 and 86, from olean-12,15-dien-3,11-diol 70, are proposed in scheme-11. Contrary to the formation of the proposed intermediates 71 and 73 (scheme—9) the double bond at C—12—13 is pushed, during the formation of the epoxide 70b from the hydroperoxide 70a towards ring E (to form a germanicol derivative) rather than to ring B or D due to the presence of double bond at C—15—16 position. Under the reaction condition the epoxide 70b is unstable due to the conformational strain caused by the double bonds at C—15—16 and C—18—19 position and hence undergoes epoxide ring opening in presence of acid forming carbonium ion 70d probably by 1,3 hydride shift from C—13 to C—11 as shown in 70c. The intermediate carbonium ion 70d undergoes ring

contraction producing the isomeric cations 70e and 70e[1], which in turn lose a proton to form isomeric aldehydes 70f and 70f[1] respectively. These aldehydes get oxidised in presence of hydrogen peroxide to the corresponding α and β carboxyllic acids at C—15 position. The α -carboxyl group in 70g being at proximity to the double bond at C—18—19, undergoes lactonisation furnishing the γ -lactone 85, whereas the intermediate 70g[1] having its carboxyl group in the β -position is at proximity to the C—15—16 double bond, lactonizes forming 86. The Dreiding model of the lactones 85 and 86, showed that the lactones are strain free, thus stabilising the molecule.

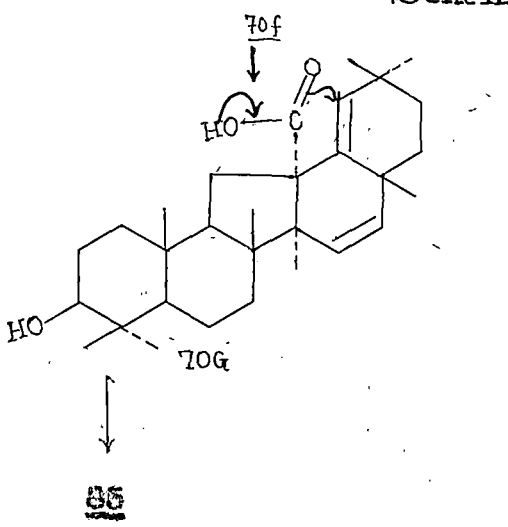
Scheme—11



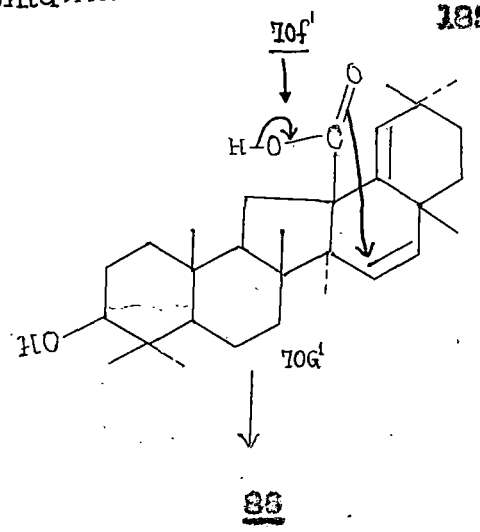
Scheme contd....



Scheme contd.....



86



88

This is perhaps the first report on the formation of a lactone with the carbon skeleton rearrangement in ring C of a triterpenoid with hydrogen peroxide in presence of p-toluene sulphonic acid which has been published by the present author[48] recently.

SECTION—B

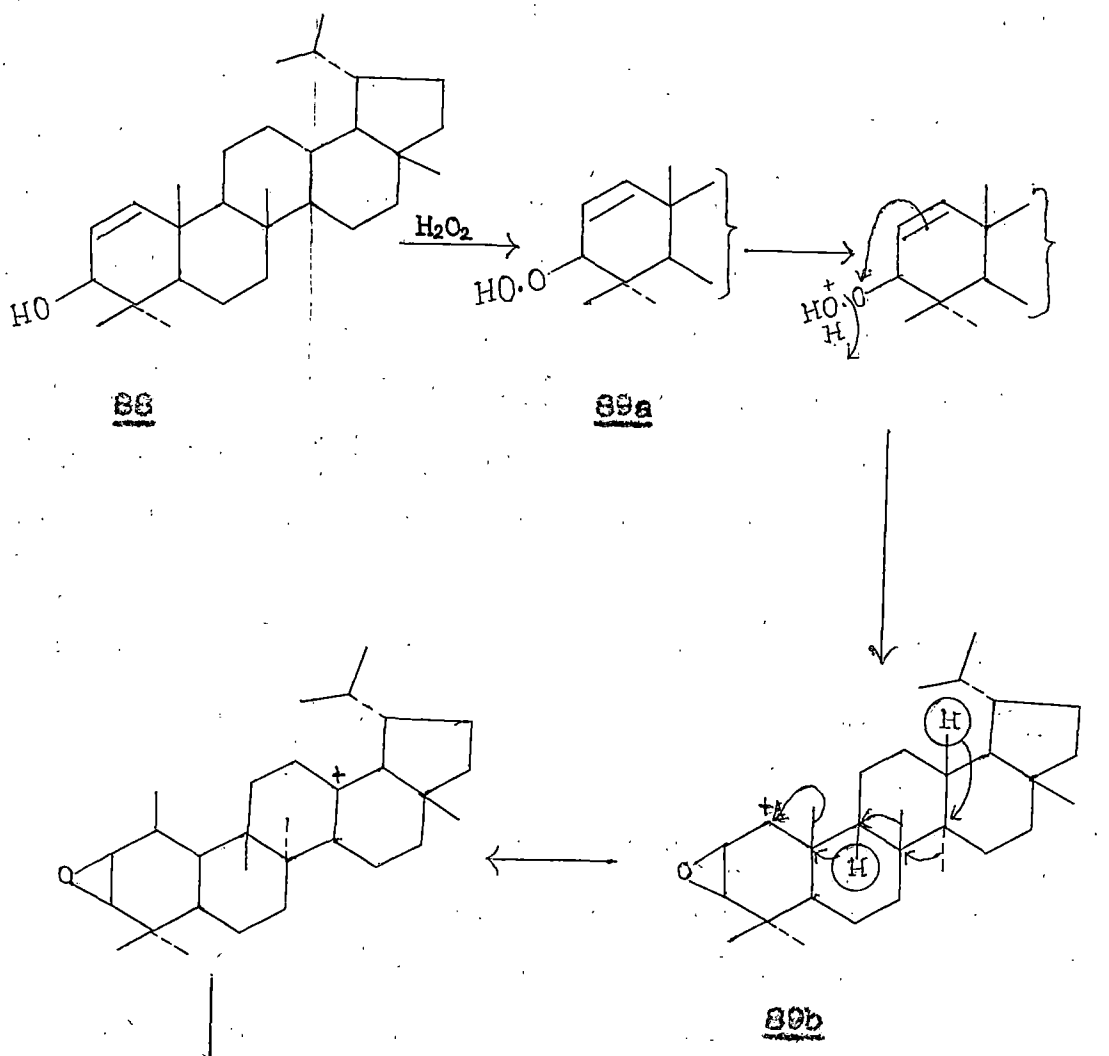
Action of hydrogen peroxide on lup-1(2)-en-3β-ol:

Introduction:

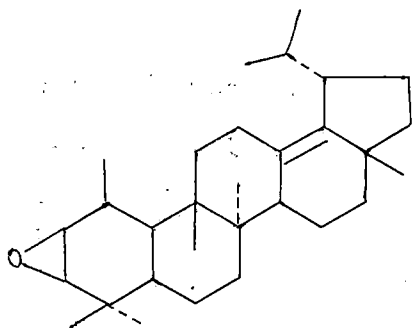
We have discussed in the section A, the action of hydrogen peroxide on olean-12,15-dien-3,11-diol 70, where the allylic alcoholic system in ring C of the triterpene furnished the interesting type of carbon rearrangement followed by lactonisation during the reaction condition. Interested by this observation, we wanted to study similar reaction on another triterpene allylic alcohol. For the model compound we selected the triterpene allylic alcoholic function in Ring A viz. lup-1(2)-en-3β-ol 88. As in the

case of olean-12,15-dien-3,11-diol if the hydroxyl group at C—3 position of lup-1,2-en-3β -ol 88 formed a hydroperoxide intermediate 89a, then it was expected to form an epoxide intermediate 89b, which could then undergo rearrangement to form 90 or 91, as shown in Scheme—12.

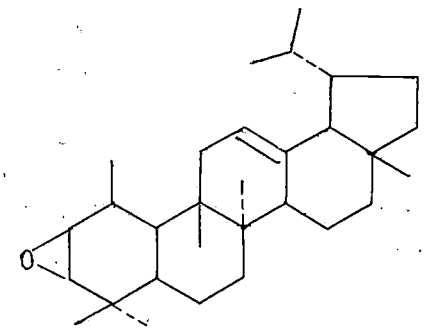
Scheme—12



Scheme contd.....



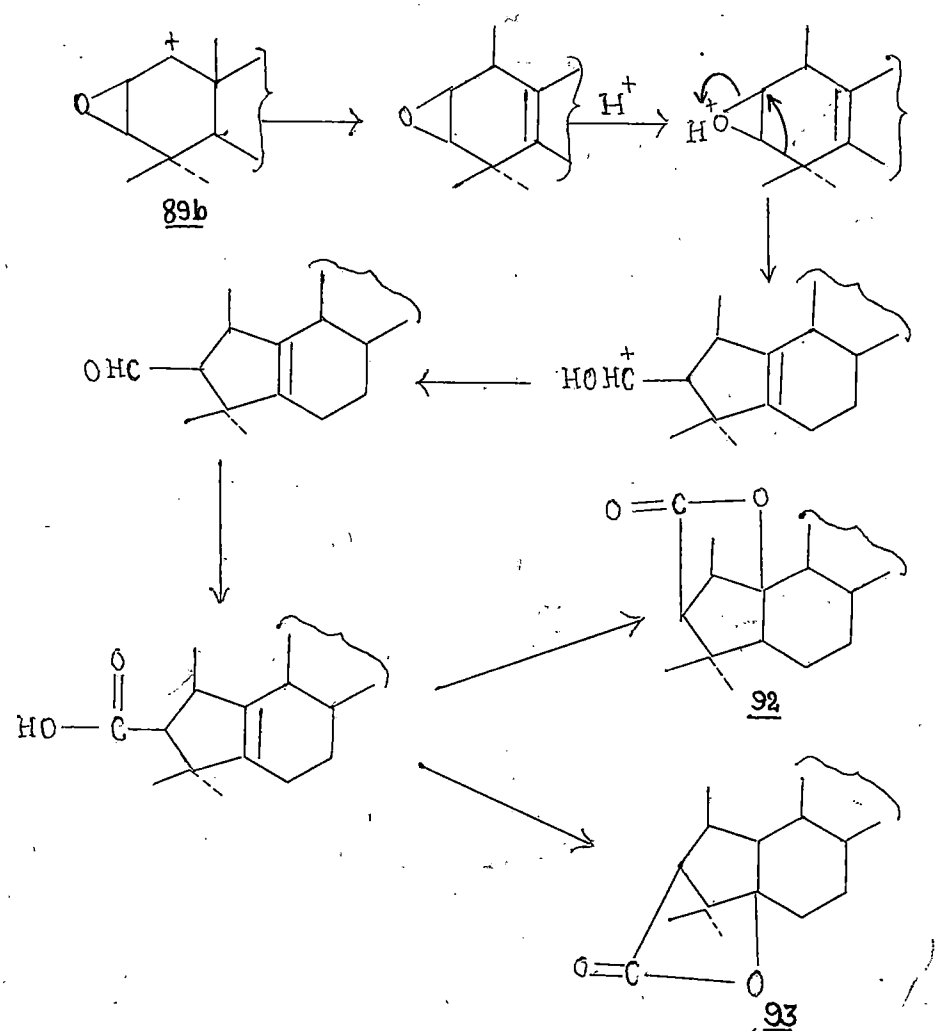
90



91

On the other hand the epoxy carbonium ion intermediate 89b may rearrange in other way to form different lactones 92 and 93 as shown in Scheme—13.

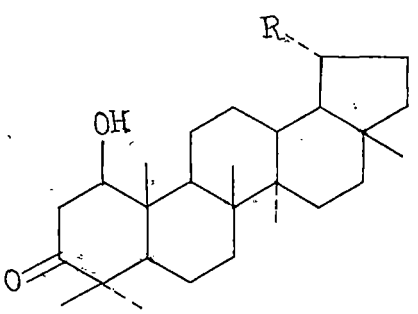
Scheme—13



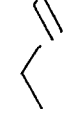
Products were expected like above (Scheme—12 & 13), but in actual practiSe the product obtained was somehow different which is discussed below:

D i s c u s s i o n:

The compound lup-1(2)-en-3β -ol 88 could not be obtained from nature. So first we had to prepare lup-1(2)-en-3β -ol 88, from a related compound which was obtained from nature. The naturally occurring compound selected was glochidonol=lup-20(29)-en-1β -ol-3-one 94, which was isolated from Glochidion-acuminatum[46]. Following the method described by Talapatra and coworkers[46], we have isolated lup-20(29)-en-1β -ol-3-one 94, from the plant Glochidion acuminatum. The glochidonol so obtained was hydrogenated



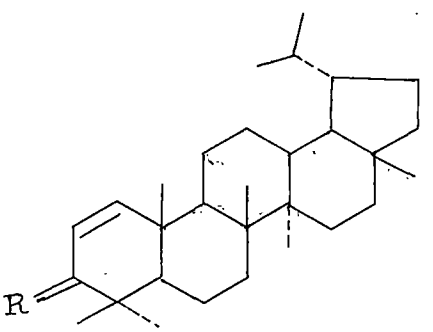
94, R = 

95, R = 

using Adam's catalyst when the isopropenyl double bond was reduced to give an amorphus solid (IR shows absence of double bond). The compound was assigned as 95.

Our aim was to prepare an allylic alcohol at ring A i.e. lup-1(2)-en-3-ol 88. So to prepare 88 from 95 first we had to dehydrate the compound 95 to produce a $\alpha-\beta$ -unsaturated ketone 96 and then reduction of 96 would give the desired product.

Dehydration of the keto alcohol 95, with acetic anhydride and pyridine by the method of Talapatra and co-workers[46], gave a solid which on chromatography followed by crystallisation yielded a compound 96, C, H analysis showed the molecular formula, $C_{30}H_{48}O$, m.p. 177—78° (lit[47] m.p. 177—179°). UV absorption of the compound showed a maxima at λ_{max} 228 nm (ϵ =18,000) which confirmed the presence of a $\alpha-\beta$ -unsaturated carbonyl functional group. IR spectrum (Fig.21) of the compound showed peaks at 1680 cm^{-1} ($\alpha-\beta$ -unsaturated ketone). The compound was identified as lup-1(2)-en-3-one, 95.



96, R = O
88, R = β-OH, α-H

The $\alpha-\beta$ -unsaturated ketone 96 so produced was reduced by lithium aluminium hydride in dry ether. After usual

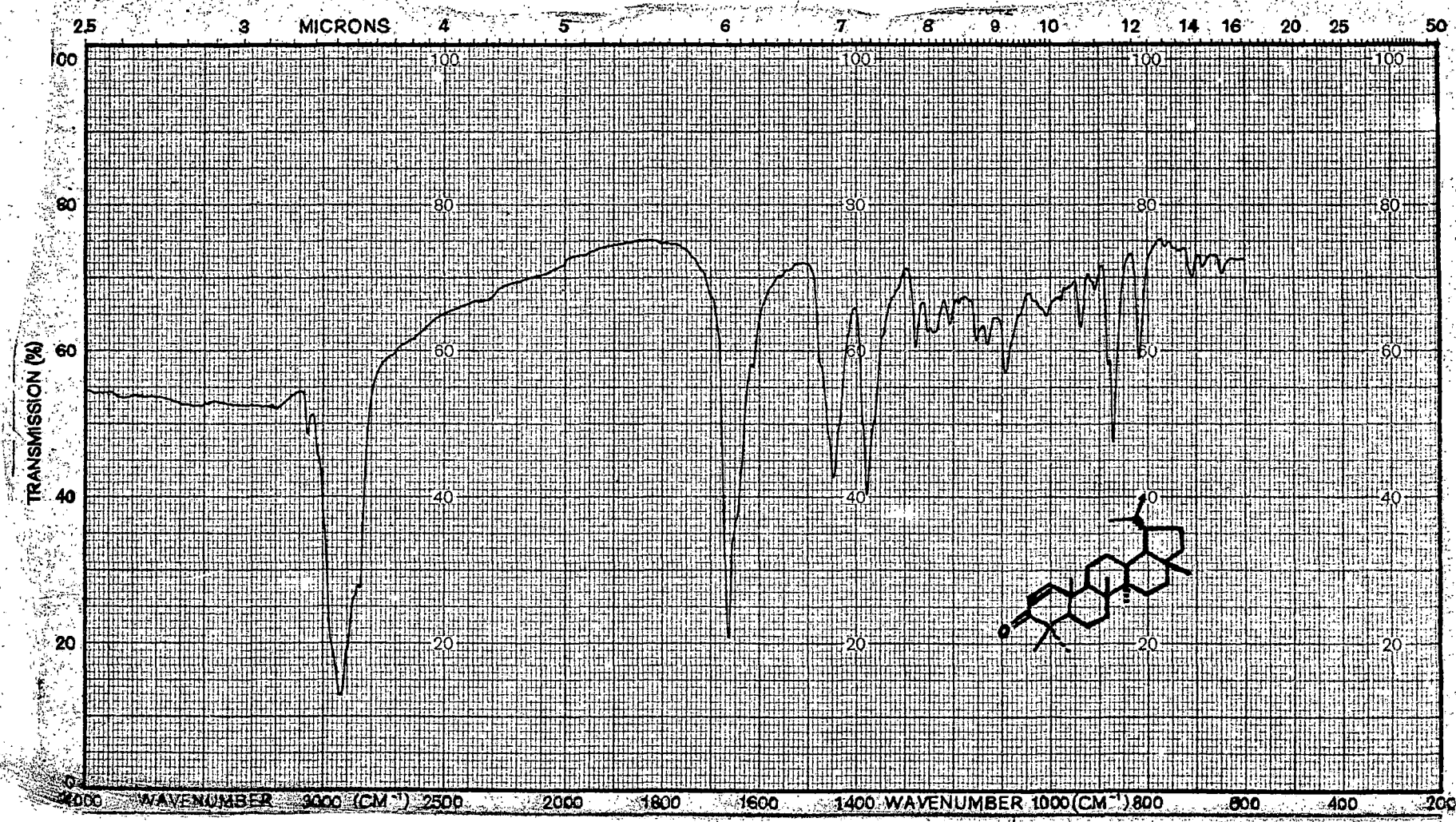


Fig.21: IR spectrum of lup-1(2)-en-3-one, 96.

work up followed by chromatography and crystallisation a compound 88, $C_{30}H_{50}O$, m.p. 314—15° was obtained. No UV absorption was recorded for the compound in the region 220—350 nm. IR spectrum (Fig.22) of the compound showed a peak at ν_{max} 3450 cm^{-1} (—OH), another peak at 880 cm^{-1} for the H—C=C—H was obtained. The ^1H NMR spectrum (Fig.23) of the compound 88 showed peaks in the region 0.7—1.01 ppm for 8-methyl groups present in the molecule. The proton attached to the C—3—OH appeared as a multiplet at 3.25 ppm with $W_{\frac{1}{2}}$ = 16Hz, indicating β-equatorial orientation of C—3 hydroxyl group. A multiplet (quartet type) centred at 4.58 ppm was due to vinyl proton at C—2 and the doublet at 4.69 was due to the vinyl proton at C—1. On the basis of above data the structure of the compound 88 was confirmed.

The allylic alcohol 88 was treated with hydrogen peroxide in presence of p-toluene sulphonic acid in tert-butyl alcohol at room temperature according to method of Corey et al[23]. After stirring for twenty four hours and then usual work up and chromatography afforded a compound 97, $C_{30}H_{50}O_3$, m.p. 280—1° was obtained. No UV absorption was observed for the compound 97. IR spectrum (Fig.24) of the compound 97 showed peaks at ν_{max} 3420 cm^{-1} (—OH) and 1695 (—COOH) cm^{-1}. The structure of 97 was established by the IR, ^1H NMR and mass spectral studies of its methyl ester 98. Esterification

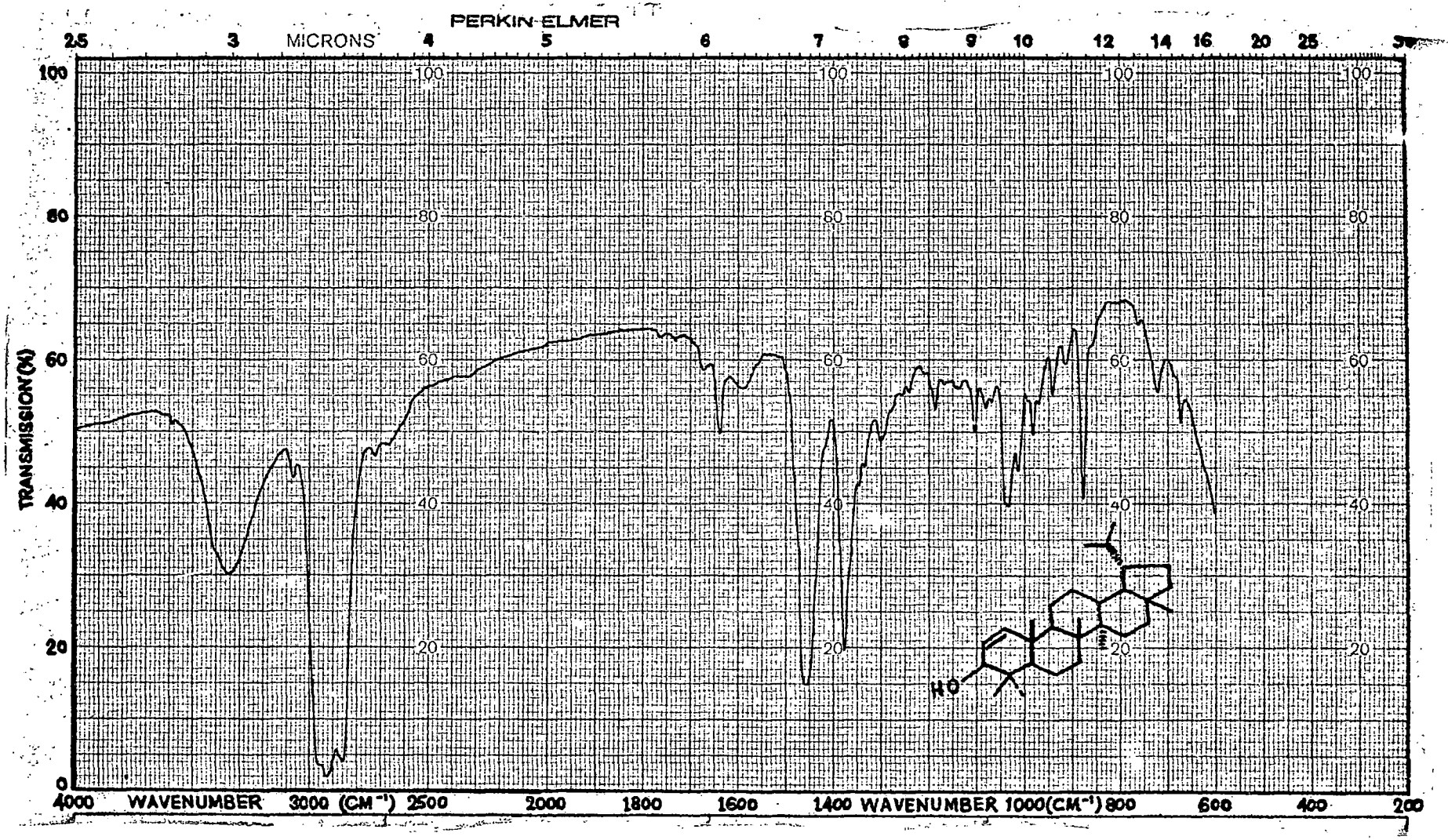


Fig.22: IR spectrum of lup-1(2)-en-3-ol, 88.

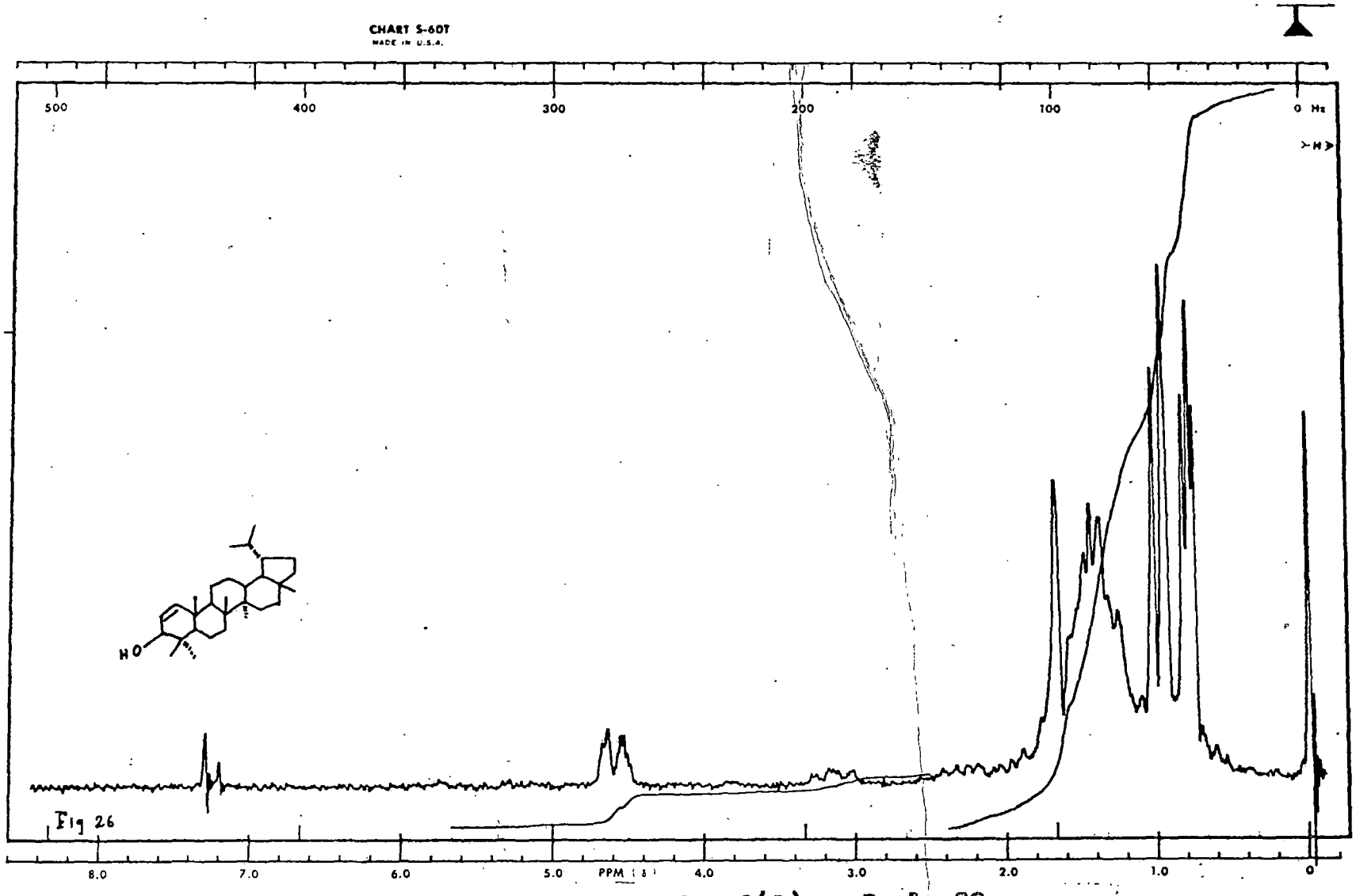


Fig.23: PMR spectrum of lup-1(2)-en-3-ol, 88.

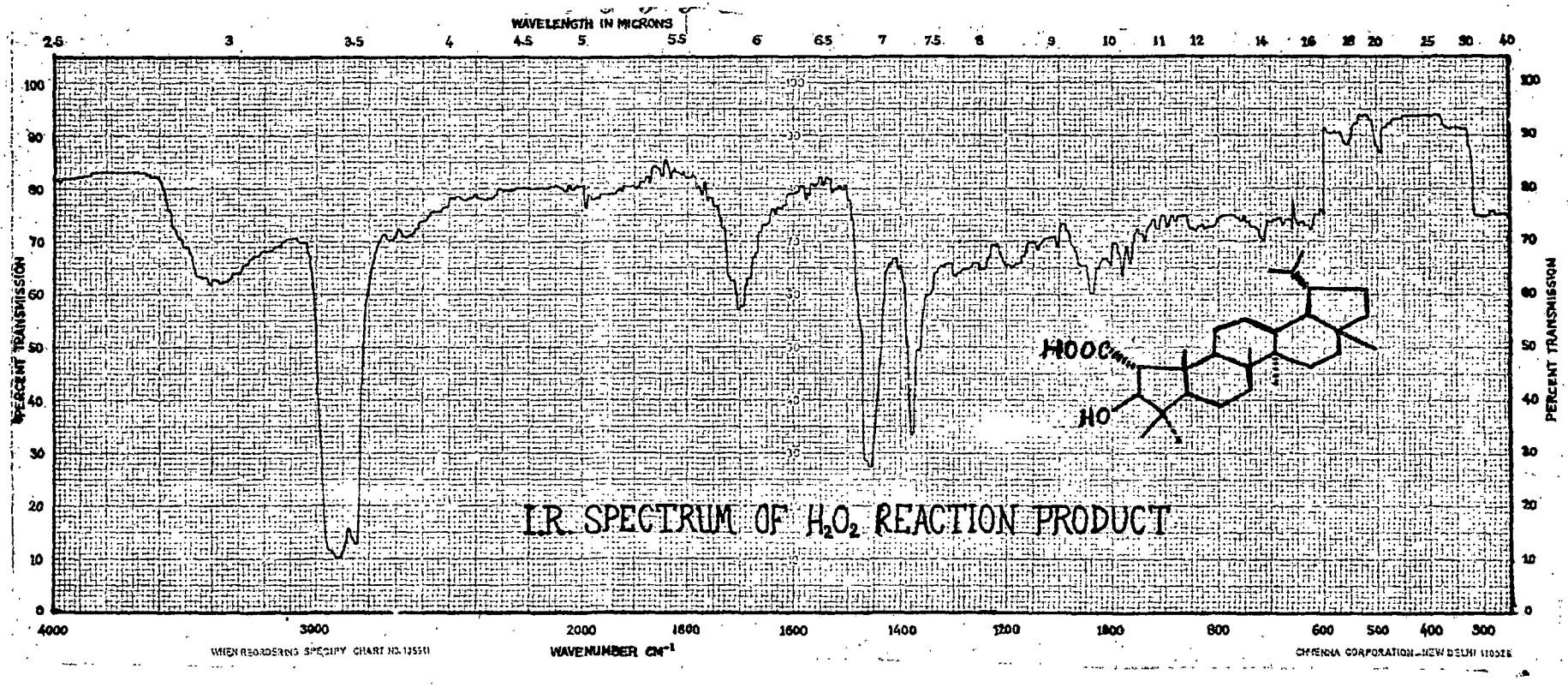
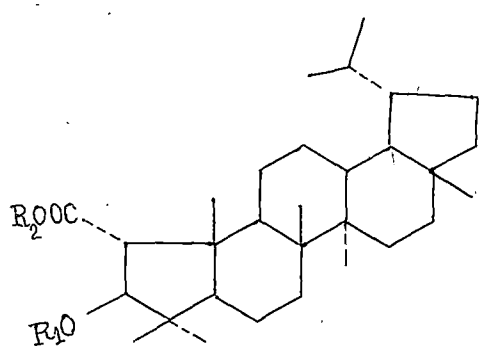


Fig.24: IR spectrum of the hydroxy acid, 57.

of the compound 97 with an ethereal solution of diazomethane afforded the corresponding methyl ester 98, $C_{31}H_{52}O_3$, of m.p. 265—66°. The structure of the methyl ester was established by its IR, ^1H NMR and mass spectral analysis. No UV absorption was observed for the compound in the region 200—350 nm. IR spectrum (Fig.25) of the compound showed peaks at ν_{max} 3380 cm^{-1} and 1735 cm^{-1} due to presence of a hydroxy and a carbomethoxy groups respectively.

^1H NMR spectrum (Fig.26) of the compound showed peaks in the region 0.8 to 1.01 ppm that was integrated for 24 protons of 8-methyl groups present in the molecule. The



97, R_1=H ; R_2=H
98, R_1=H ; R_2=CH_3
99, R_1=Ac; R_2=CH_3

peak obtained at 2.75 ppm was due to proton geminal to the carbomethoxy group (CH_3-O-CO-C<u>H</u>) which was axial from its high J-value (12 Hz) that coupled with the neighbouring proton which was α-axial, that appeared as multiplet in

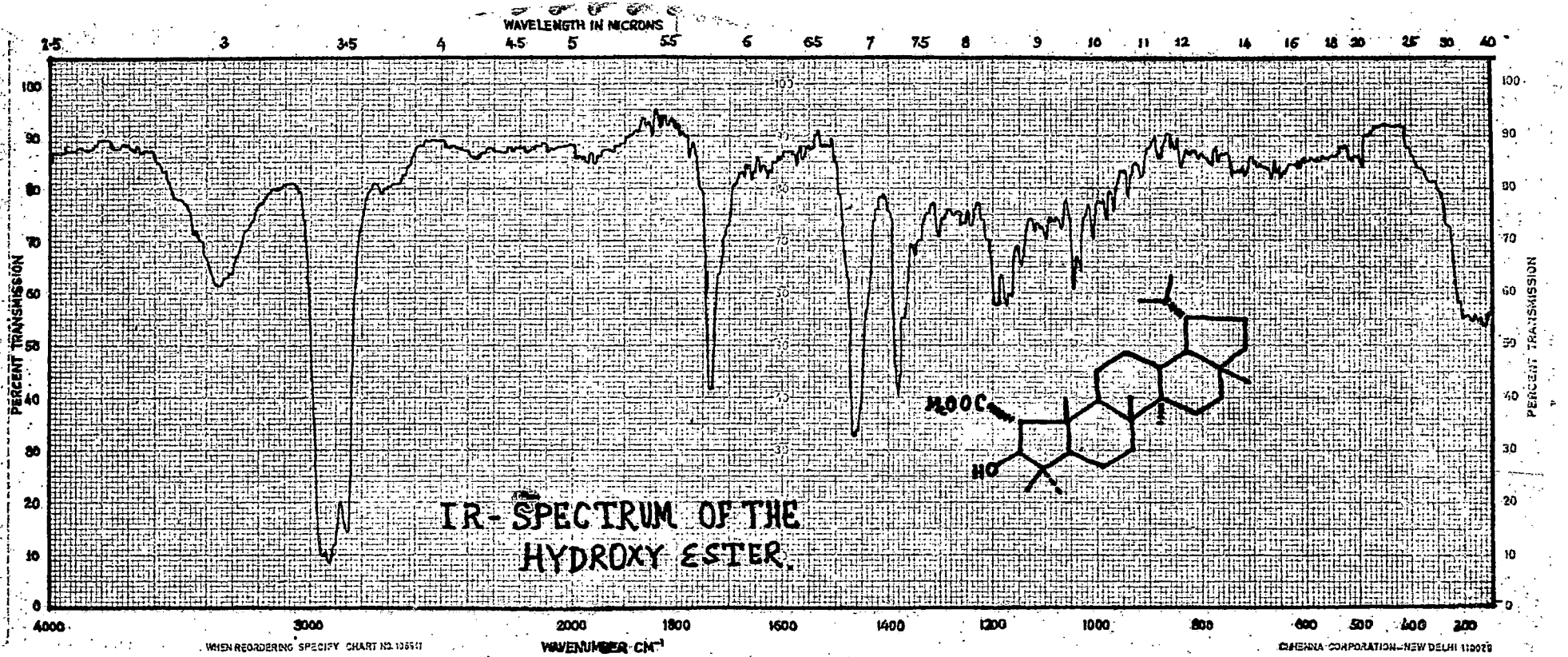


Fig.25: IR spectrum of the hydroxy ester, 98.

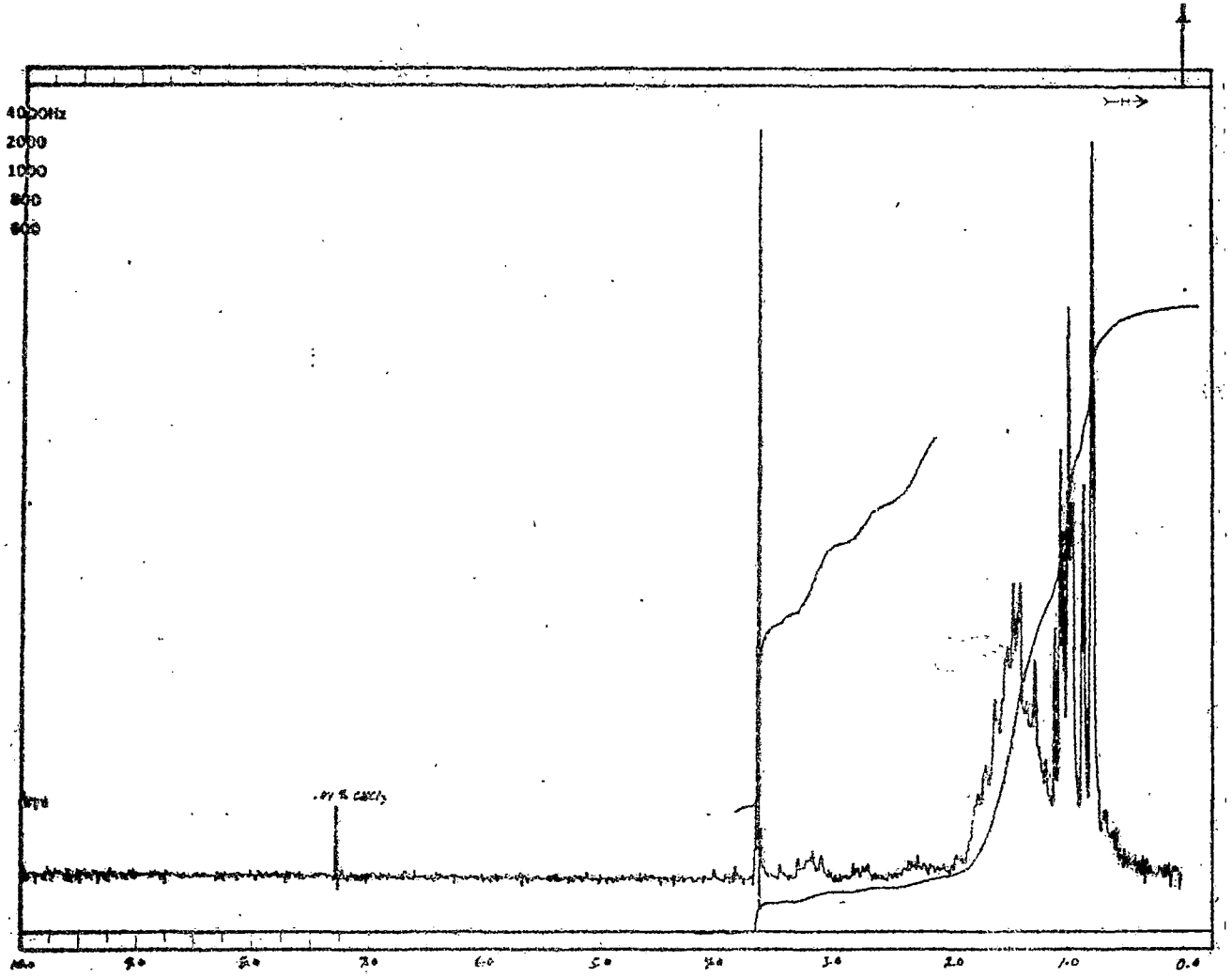
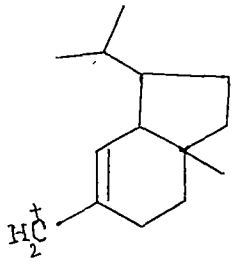


Fig.26: PMR spectrum of the hydroxy ester, 98.

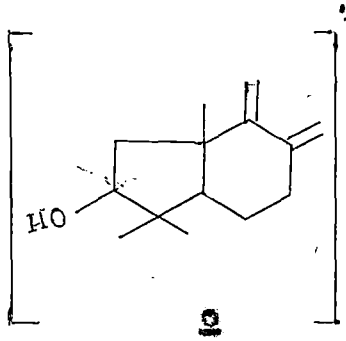
the region 3.2 ppm with the same J-value. The methyl protons in $-COOCH_3$ gave a singlet at 3.65 ppm integrated for three protons. On the basis of ^1H NMR data the structure of the hydroxy ester could be assigned as 98. The structure was finally proved by mass spectral analysis.

Mass spectrum (Fig.27) of the compound 98 showed peak at m/e 473 (MH^+) which was consistent with the molecular formula $C_{31}H_{52}O_3$, other peaks at m/e 455 (base) for MH^+-H_2O, 454 (M^+-H_2O), 439 (m/e 454—CH_3), 411(454—isopropyl), 395(454—$COOCH_3$), 251, 235, 205, 191 were observed. The fragment at m/e 191 could be characterised as the fragment of saturated lupane skeleton[43] by the species m, whereas the fragment at m/e 251 for the species g and m/e 235 by the loss of water from g; The fragment at m/e 205 could be explained by the ion fragment o without the isopropyl group.



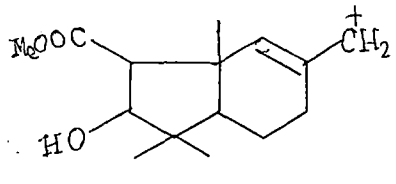
m

m/e 191



o

m/e 205



g

m/e 251

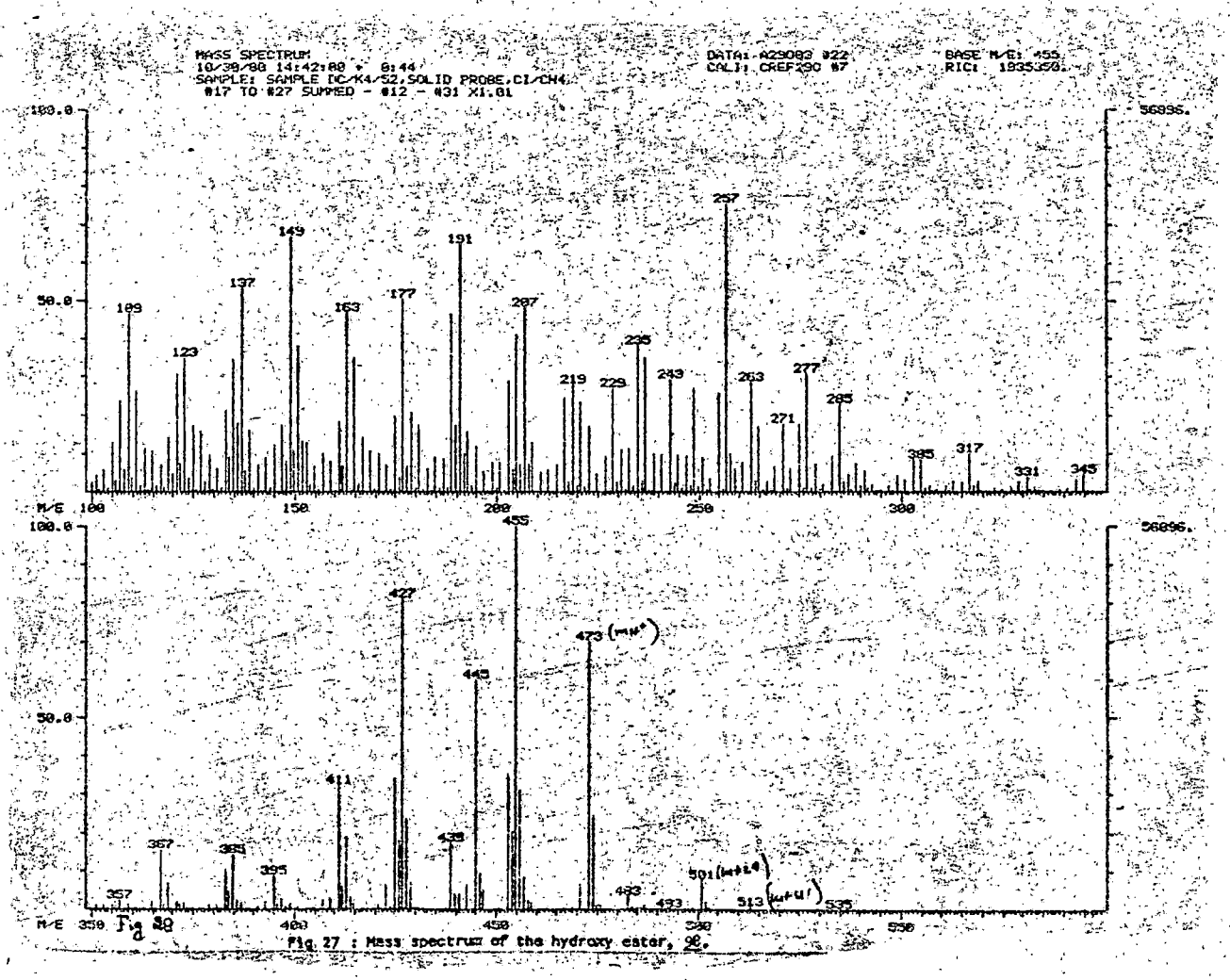


Fig 27 : Mass spectrum of the hydroxy ester, 9c.

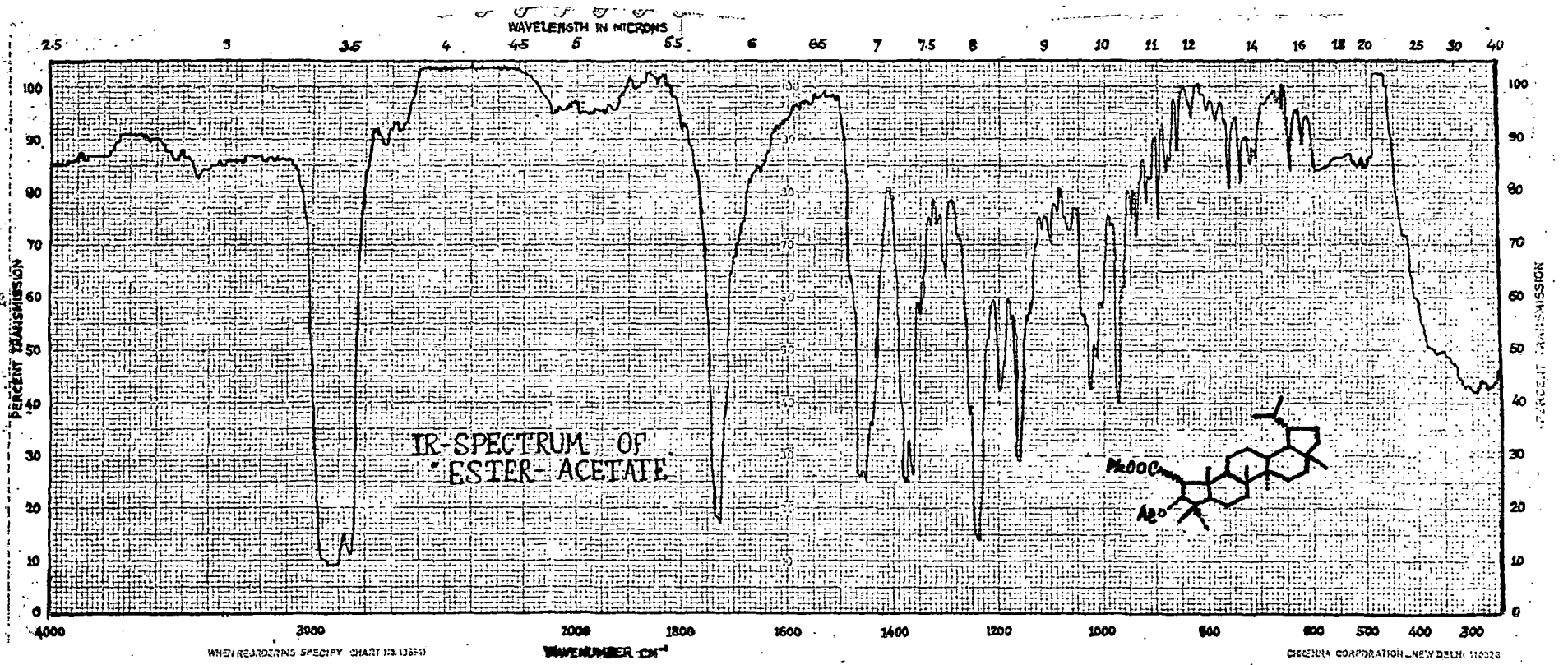


Fig.28: IR spectrum of ester acetate, 99.

Acetylation of the hydroxy ester 98, with acetic-anhydride and pyridine at room temperature gave the ester acetate which after crystallisation from chloroform-methanol mixture afforded 99, $C_{33}H_{54}O_4$, m.p. 250—1°. IR spectrum (Fig.28) of the compound showed a broad maxima at the region ν_{max} 1700—1740 cm^{-1} which was due to presence of acetoxy and ester group both. A peak at 1240 cm^{-1} confirmed the presence of an acetoxy functional group.

Mechanism of formation of hydroxy acid 97:

In the section (A), the effect of hydrogen peroxide on olean-12,15-dien-3,11-diol 70 was discussed, where the epoxide was formed from the hydroperoxide (Scheme—11) but not directly on C—12—13 double bond. The double bond at C—12—13 position was too much sterically hindered due to the ring juncture along with different sterical effect of C—17 and C—14 CH_3 groups. The double bond was known to be very stable in ordinary reagents. But in the compound lup-1(2)-en-3-ol 38, the epoxide could be formed directly on C—1—2 double bond because the double bond was not too much sterically hindered. Govindachari et al[47] reported that the formation of epoxide on lup-1(2)-en-3-one could be done easily with alkaline hydrogen peroxide. From this idea we have schemed the mechanism as follows (Scheme—14):

First there would be a formation of 3β-hydroxy-epoxide as intermediate 100. The epoxide 100, so formed would be opened in presence of acid and carbonium ion 101 would be formed. The carbonium ion intermediate could undergo ring contraction producing the cation 102, which in turn loses one proton to form the aldehyde 103 and during reaction condition it would be oxidised to the corresponding hydroxy acid 97.

Scheme—14