## OXIDATION OF FRIEDELAN-3-ONE WITH META CHLOROPERBENZOIC ACID IN CHLOROFORM SOLUTION.

Pentacyclic triterpenoids undergo various types of oxidative rearrangement reactions on treatment with metachloroperbenzoic acid giving rise to functionalisation[24] at unactivated carbon atoms or seco acids[29] when there is catalytic amount of para toluenesulfonic acid. So the author have carried out the reaction of meta chloroperbenzoic acid on triterpenoid ketones having 4-mono methyl system in ring-A taking friedelan-3-one **30** and 3-oxo friedelan 27 15-olide **53** with the aim to examine the nature of products formed.

### OXIDATION OF FRIEDELAN-3-ONE **30** :

A solution of friedelan-3-one **30** in chloroform and meta chloroperbenzoic acid was refluxed for 6 hours over waterbath. After usual workup, it was diluted with extra chloroform and separated into neutral and alkali parts. The neutral part gave a gummy mass which was chromatographed and on elution with petrol-benzene (3:2) a solid mass, compound-A was obtained. The alkali part on acidification with hydrochloric acid (20%) gave a white substance identified as m-chlorobenzoic acid, *M.P.*157-8°C.

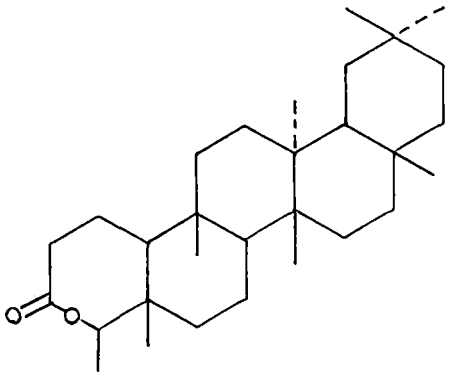
### Identification of compound-A :

Compound-A was crystallised from chloroform-methanol, *M.P.*271-2°C; Its IR spectrum (fig.1) showed absorption peak at 1720 $cm^{-1}$ probably due to $\varepsilon$-lactone carbonyl group. Mass spectrum (fig.2) showed molecular ion peak at m/e 442 $(M,38)^{+}$, other peaks appeared at 427 (14), 398 (70), 383, 274, 245, 218, 205, 123, 109, 95 (100). Elemental analysis and Mass spectrum showed the molecular formula to be $C_{30}H_{50}O_2$.

Its $^{1}H$ NMR spectrum (fig.3) showed seven singlets of 3H each ($\delta$ in ppm.) at 0.82, 0.88, 0.93, 0.98, 0.99, 1.00 and 1.18; a doublet

that appeared at 1.20 (J= 6.5 Hz) was due to C-4 methyl group. The quartet centred at 4.23 (J= 6.5 Hz, 1:3:3:1) was accounted for the methine proton attached at C-4 and the multiplet around 2.60 was due to methylene protons at C-2.

The compound-A has been found to be identical with friedelan 3→4-olide 32 by direct comparison (co-tlc,co-IR and *M.M.P.*) with authentic sample.



32

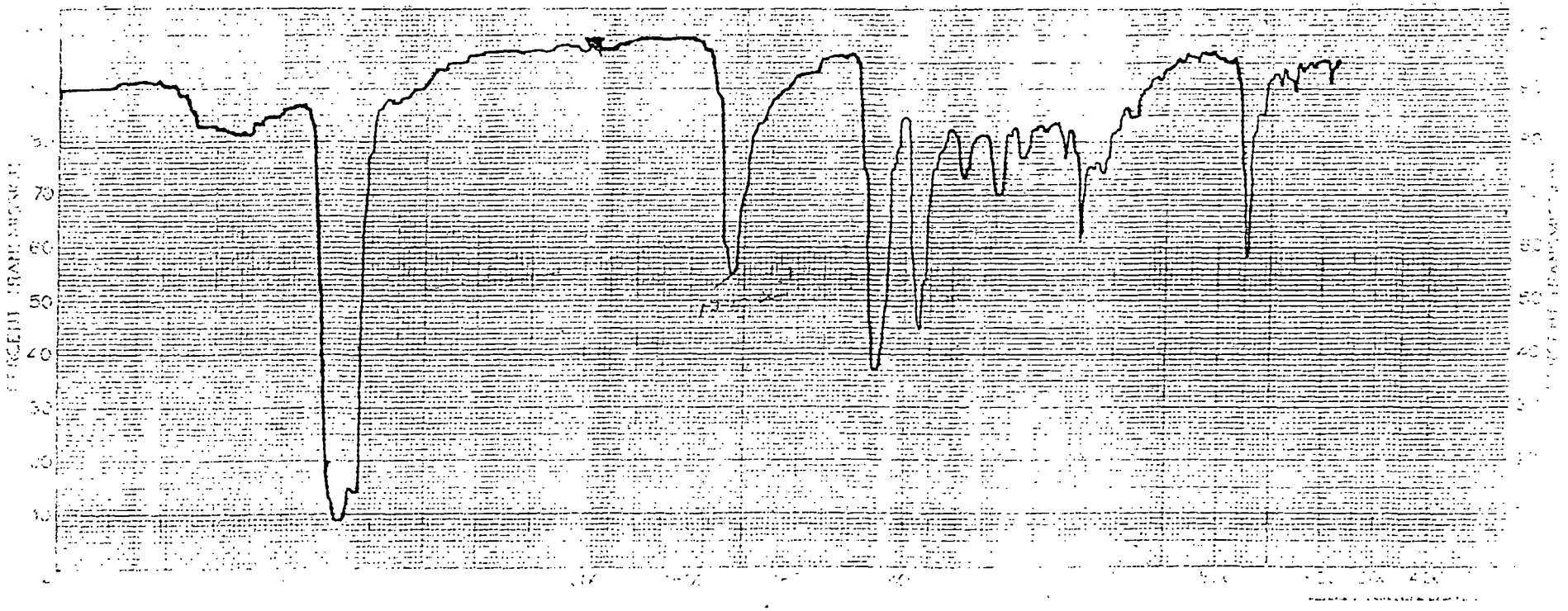


Fig. 1, IR spectrum of seco friedel-3→4-olide, 32.

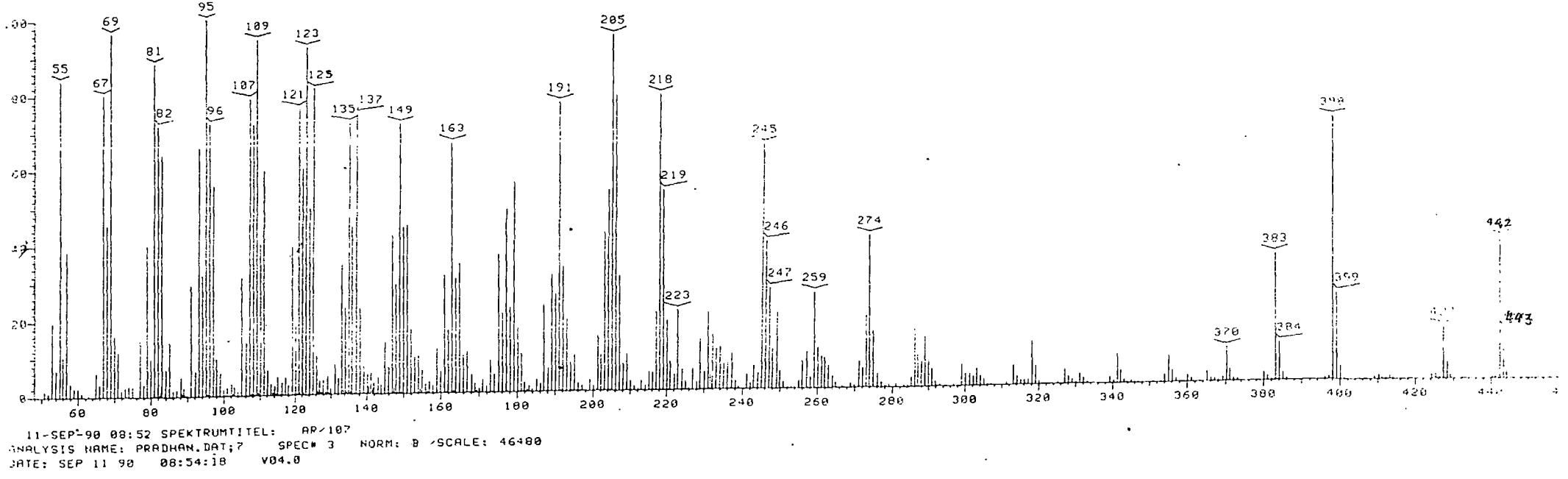



Fig. 2, Mass spectrum of seco friedel-3→4-olide, 32.

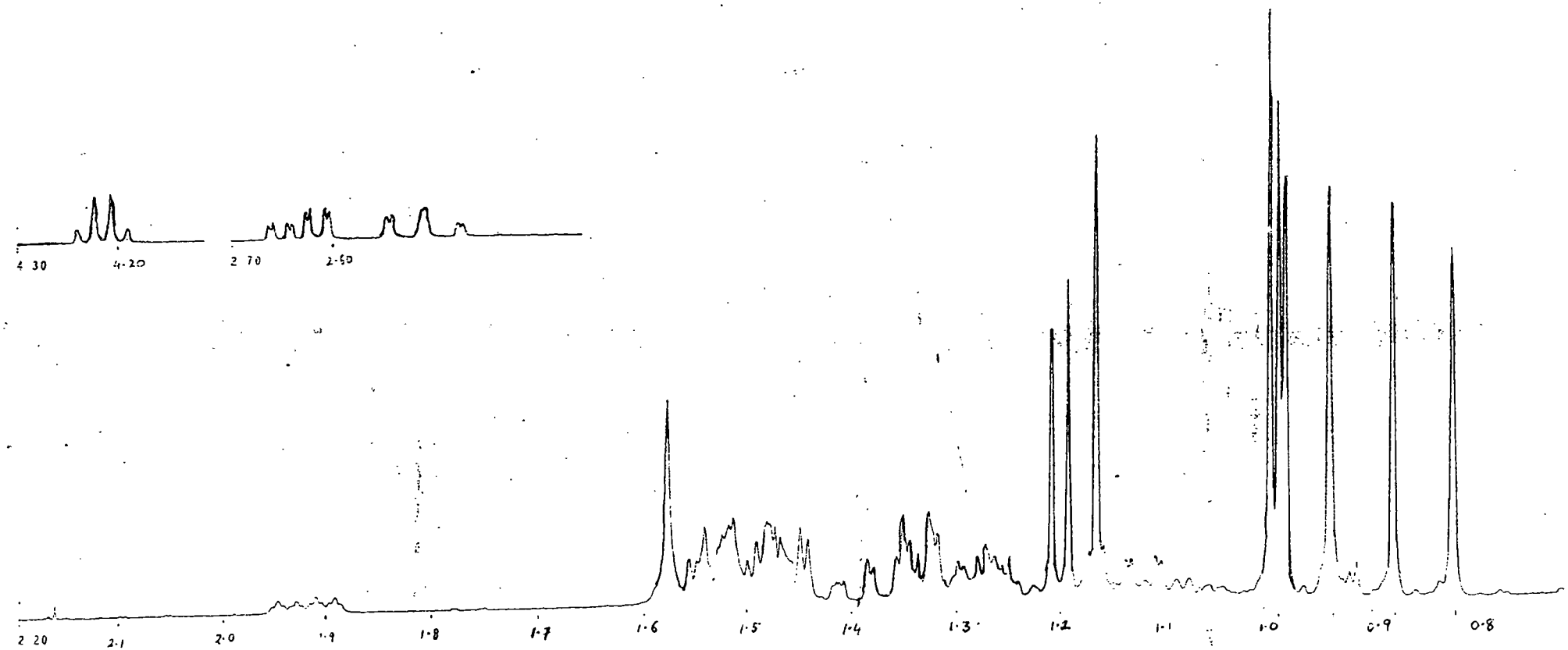



Fig. 3, $^{1}H$ NMR spectrum of seco friedel-3→4-olide, 32.

## OXIDATION OF 3-OXO FRIEDELAN 27→15-OLIDE (ODOLACTONE) WITH META-CHLOROPERBENZOIC ACID IN CHLOROFORM.

3-oxo friedelan 27→15-olide **53** was dissolved in chloroform followed by addition of meta chloroperbenzoic acid and the mixture was refluxed for 6 hours. After workup, it was diluted with chloroform and separated into neutral and alkali parts. The gummy product obtained from the neutral part was chromatographed, which on elution withpetrol-benzene (1:4) furnished a white substance as compound-B.

The alkali part on acidification with hydrochloric acid (20%) gave a white solid mass which was identified as meta chlorobenzoic acid, *M.P.* 157-8°C.

### Identification of compound-B :-

Compound-B was crystallised from chloroform-methanol repeatedly to furnish crystalline solid, *M.P.*> 300°C. IR spectrum (fig.4) showed absorption peaks at 1730 and 1760 $cm^{-1}$ indicating the presence of $\varepsilon$-lactone and $\gamma$-lactone rings. Mass spectrum (fig.5) showed molecular ion peak at m/e 470 (M,1%)$^{+}$, other important peaks observed were at 426 (20), 408, 383, 363, 123 (100). The molecular formula was calculated to be $C_{30}H_{46}O_4$.

The $^{1}H$ NMR spectrum (fig.6) resonance signals of compound-B are recorded in tabular form in table-I below :-

*TABLE-I.*

| Chemical shifts. ($\delta$ in ppm.) | No. of protons. | multiplicity | Assignments. |
|---|---|---|---|
| 0.85 | 3 | singlet | |
| 0.90 | 3 | " | |

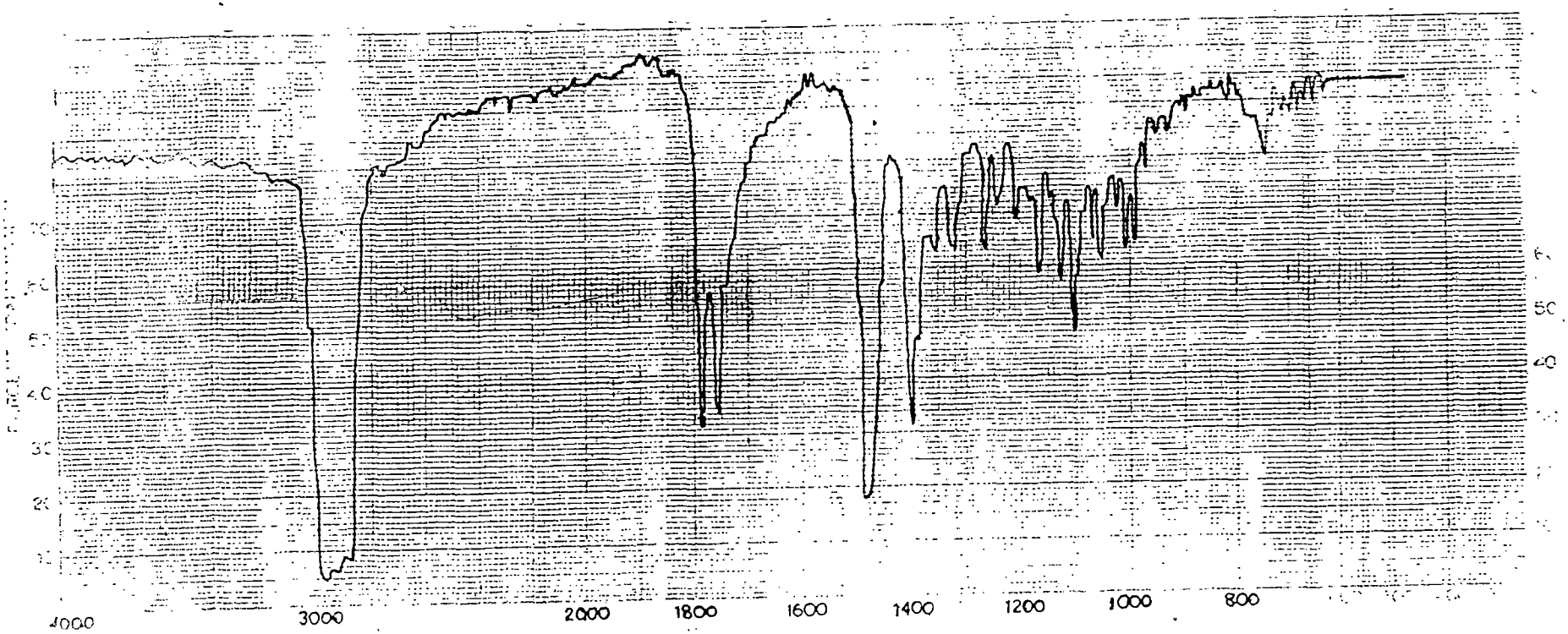



Fig. 4, IR spectrum of friedel-3→4, 27→15-di-olide, 54.

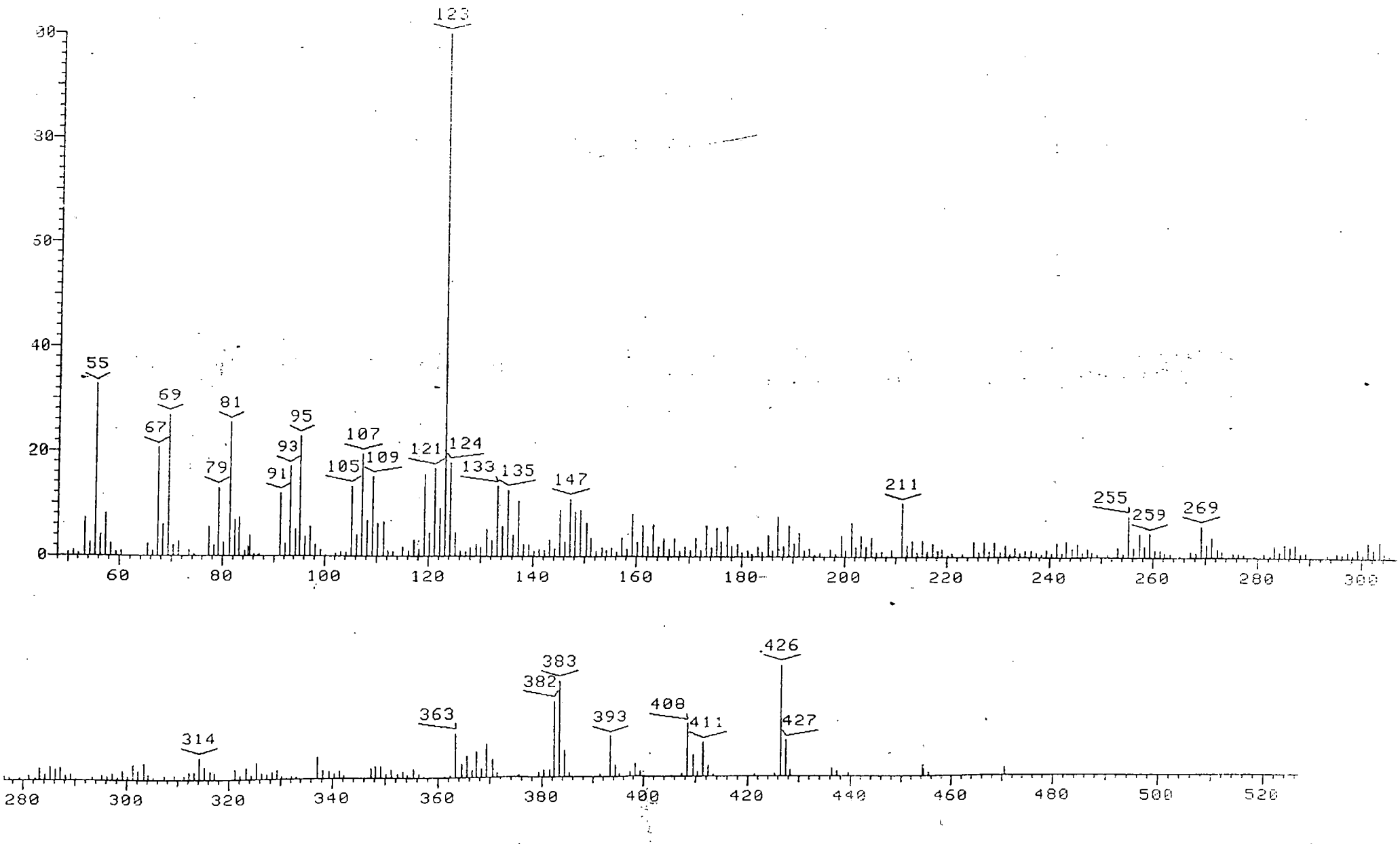



Fig. 5, Mass spectrum of friedel-3→4, 27→15-di-olide, 54.

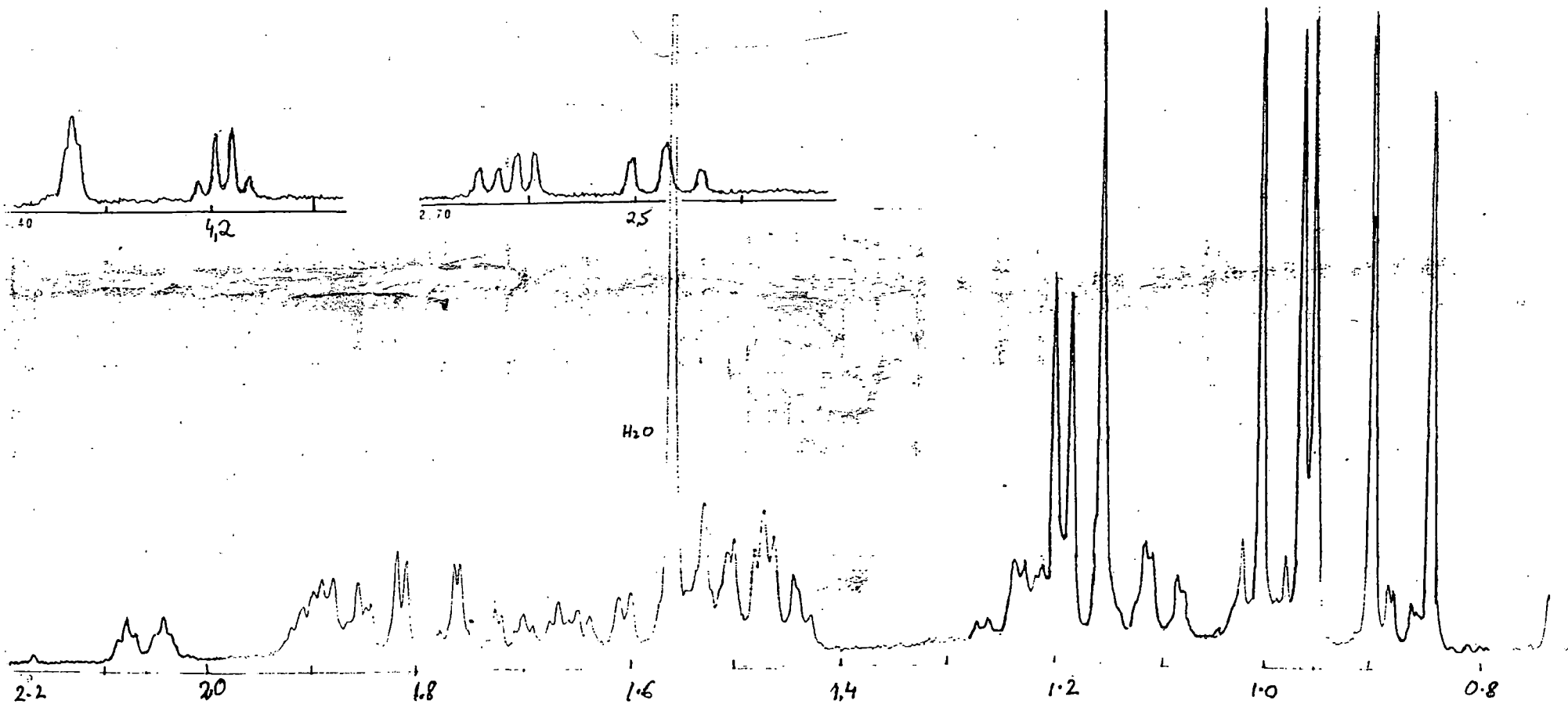
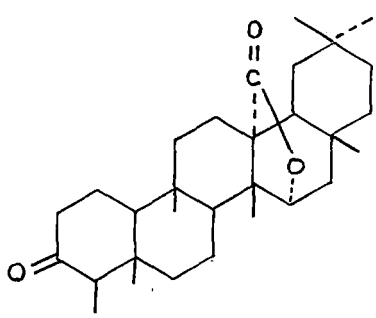


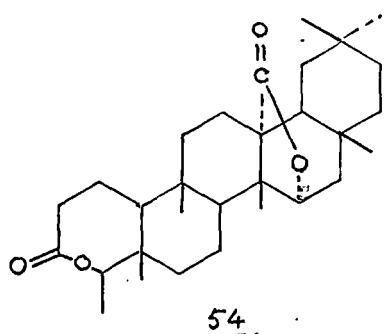

Fig. 6, $^{1}H$ NMR spectrum of friedel-3→4, 27→15-di-olide, 54.

| | | | |
|---|---|---|---|
| 0.95 | 3 | " | 6X t-$CH_3$ |
| 0.96 | 3 | " | |
| 1.00 | 3 | " | |
| 1.16 | 3 | " | |
| 1.20 | 3 | doublet (J= 6.5 Hz) | $CH_3$-$C_4$H- |
| 2.46 | 1 | multiplet | 2α-H |
| 2.63 | 1 | " | 2β-H |
| 4.19 | 1 | quartet (J= 6.5 Hz) | $C_4$-H |
| 4.35 | 1 | triplet (J= 3 Hz) | 15β-H |

Hence, from the spectral studies it was concluded that compound-B posses the structure friedelan 3→4,27→15 di-olide **54**.



**53**



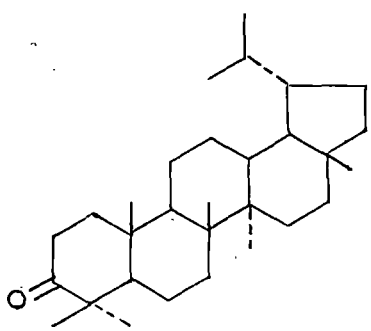
**54**

*ATTEMPTED OXIDATION OF PENTACYCLIC TRITERPENOID KETONES HAVING 4,4 -DIMETHYL SYSTEM IN RING-A WITH META CHLOROPERBENZOIC ACID.*

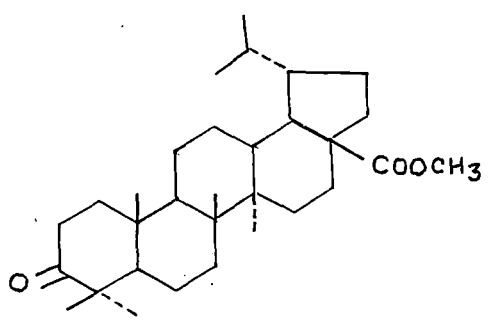
The reaction of m-chloroperbenzoic acid on compound **30** and **53** having one methyl group at C-4 encouraged the author to extend the reaction on compounds having dimethyl system at C-4. Lupanone **22** and methyl dihydrobetulonate **55** was taken as substrates of that system. But on carrying out the same reaction with m-chloroperbenzoic acid under identical conditions it was found that there was no lactone formation in ring-A in contrary to our previous observation (section A and B of this chapter).

The probable reason may be that geminal methyl groups at C-4 increases the steric hindrance which in turn hinders the lactone formation in ring-A between $C_4$ $C_3$.

These observations indicate that with m-chloroperbenzoic though Baeyer-Villiger reaction takes place in case of 4-mono substituted 3-keto triterpenoid viz. friedelin **30**, the oxidation do not occur in 4,4-disubstituted 3-keto triterpenoid viz. lupanone **22** and methyl dihydro betulonate **55**. However, the reaction proceeds smoothly in presence of p-toluenesulphonic acid as observed by Pradhan et al.[29] Further it also shows that the functionalisation of C-19,C-15 carbons by m-chloroperbenzoic acid do not occur in these systems as reported by Motoo Tori et al.[24]




**22**




**55**

## OXIDATION OF ACETYL METHYL BETULINATE WITH META CHLOROPERBENZOIC ACID IN CHLOROFORM.

A solution of acetyl methyl betulinate **56** in chloroform and meta chloroperbenzoic acid was refluxed for 6 hours. After workup and chromatography two different products C and D were obtained on elution with benzene-petrol (4:1) and benzene-chloroform (4:1) respectively.

### Identification of compound C :-

Compound C was crystallised from chloroform-methanol, *M.P.* 151-2°C. Its IR spectrum (fig.7) showed absorption peaks at 1740 $cm^{-1}$ (broad) probably due to overlapping of more than one carbonyl groups and at 1250 $cm^{-1}$ characterstic for the acetate function.

Mass spectrum (fig.8) indicated molecular ion peak at m/e 544 ($M^+$) while the other peaks observed were at 498 (M -HCOOH,26)$^+$,484 (M-AcOH, 42)$^+$,438 (54), 423 (23), 410 (22),395 (22), 379 (22), 249 (30), 189 (100). Elemental analysis and Mass spectrum suggests the molecular formula to be $C_{33}H_{54}O_6$, which when compared to that of starting material acetyl methyl betulinate **56** ($C_{33}H_{54}O_4$),showed that there is introduction of two atoms of oxygen in the molecule, to form compound -C. The negetive TNM test and absence of absorption at 3020-3040, 1640 and 890 $cm^{-1}$ showed the loss of unsaturation indicating that the group $C=CH_2$ is converted to either HC-COOH or HC-OCHO groupings. Again, the absence of absorption peak at 1690-1700 and 2700-3300 $cm^{-1}$ in IR spectrum (fig.7) showed that the carboxyl group is absent in compound C. So the formate group (O-CHO) is the probable function to fit in compound C. This deduction is well documented by $^1H$ NMR (fig.9) spectral analysis.

The $^1H$ NMR (fig.9)spectrum showed the presence of five tertiary methyls in the region ($\delta$ in ppm.) 0.8 to 0.96; two doublets centred at 1.19 and 1.22 integrated together for three protons in the ratio 11:9 had the same coupling constant of 7 Hz is probably due to the secondary methyl at C-30 carbon. The acetate methyl at C-3 and the

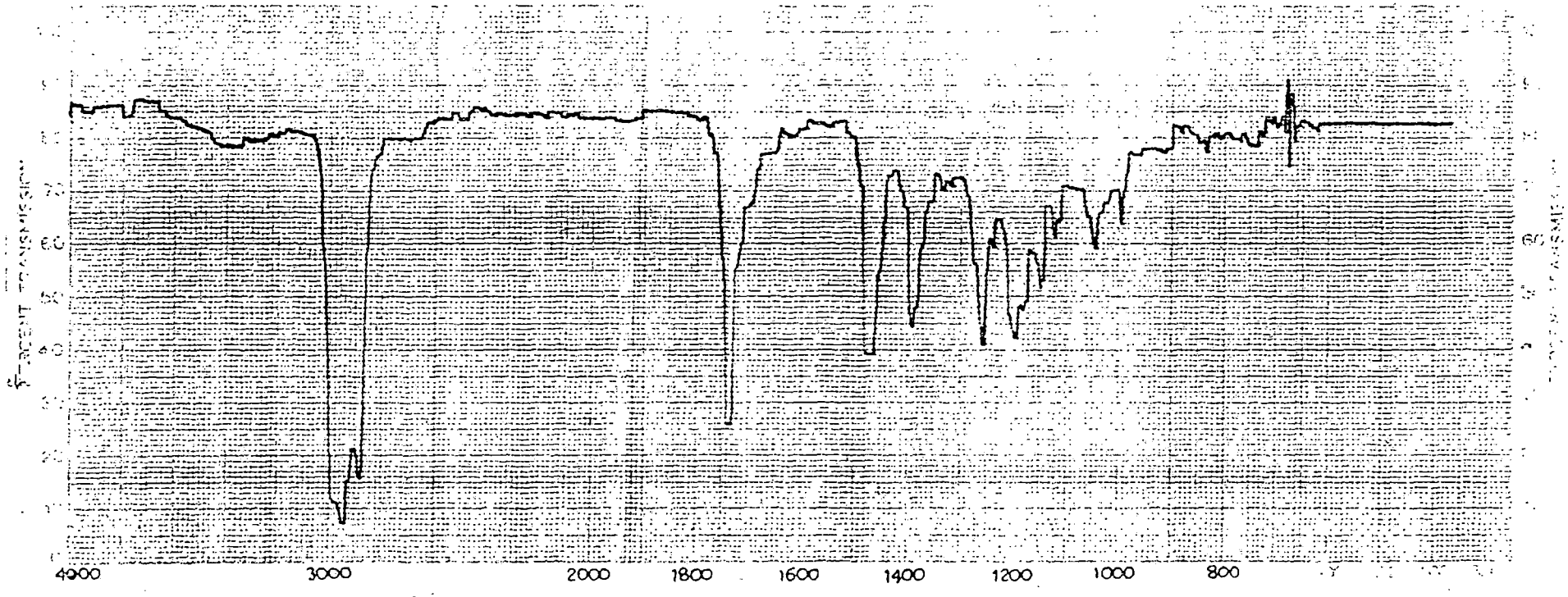



Fig. 7, IR spectrum of 29-nor 3β-O--acetyl-Lupan-20-O-formyl 28-methyl carboxylate, 57a.

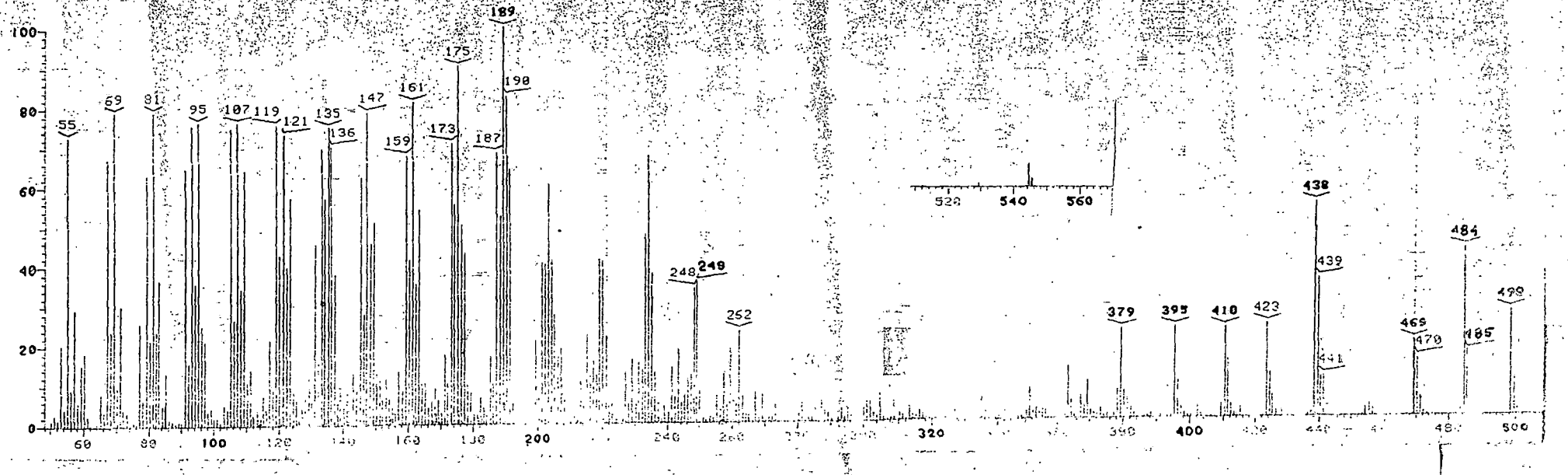



Fig. 8, Mass spectrum of 29-nor 3β-O--acetyl-Lupan-20-O-formyl 28-methyl carboxylate, 57a.

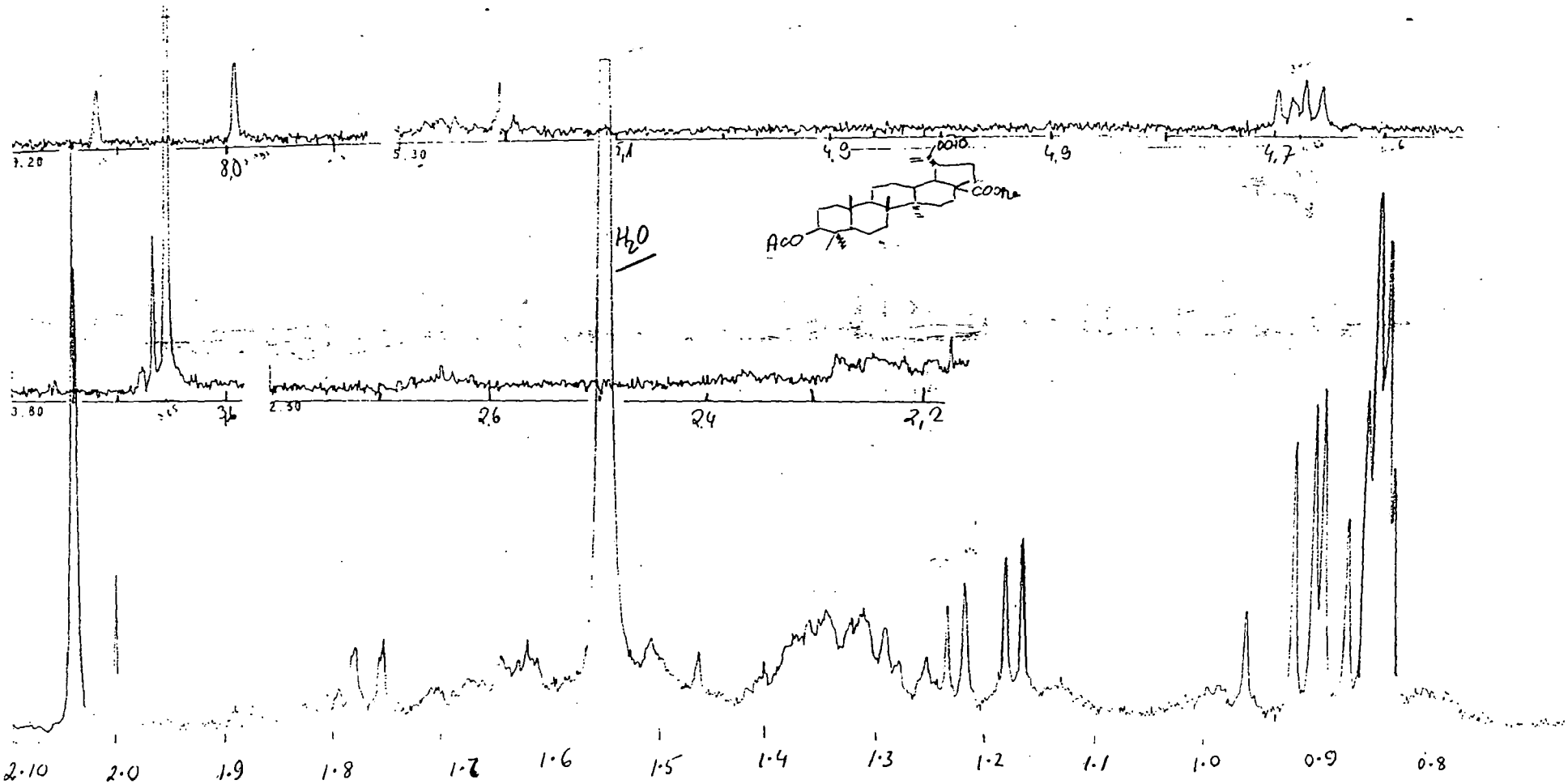
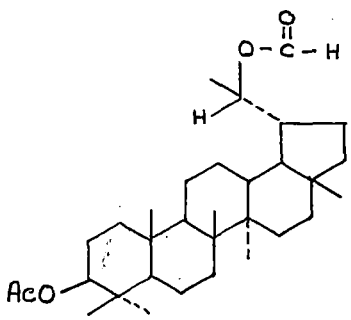


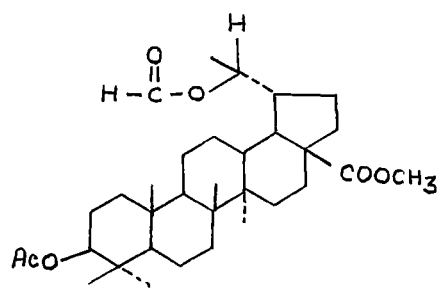

Fig. 9, $^{1}H$ NMR spectrum of 29-nor 3β-O--acetyl-Lupan-20-O-formyl 28-methyl carboxylate, 57a.

corresponding geminal proton appeared at 2.06 and 4.45 along with the carbomethoxyl group of C-28 at 3.68; The multiplet at 5.2 integrated for a proton must be due to the proton attached at C-20 carbon that has a geminal oxygen function as indicated by the IR spectrum.
The existance of two downfield singlets at 7.99 and 8.12 ppm integrated for a single proton in the ratio 11:9 indicated that the proton is due to a formyl proton which possibly have two different stereochemical geometry.

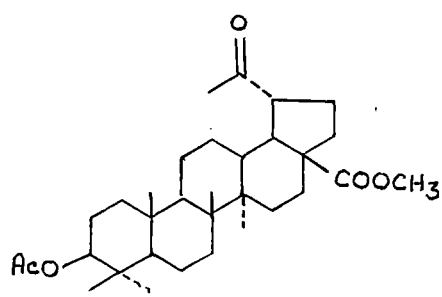
Thus, from all the above spectral analysis the structure can be awarded to compound-C as 29-nor 3β-O-acetyl-lupan-20-O-formyl-28-methyl carboxylate **57a**.




57a




57b




58

The existance of two sets of peaks for the C-30 methyl and formyl protons along with the other peaks for the tertiary methyls would be explained if an isomeric form of the side chain is possible for free existance as **57b**.

Compound-D :

It was crystallised from chloroform-methanol, *M.P.*211-2°C ;The IR spectrum (fig.**10**) showed a broad absorption peak at 1730 $cm^{-1}$ possibly due to merger of carbonyl groups of acetate and ester function while the other at 1260 $cm^{-1}$ is characterstic of acetate group. Its molecular formula is calculated to be $C_{32}H_{50}O_5$ from elemental and mass analysis. Mass spectrum (fig.**11**) showed molecular ion peak at m/e 514 $(M,2)^+$, in addition to other peaks at 454 $(M-AcOH,36)^+$, 439 (14),411 (20), 395 (6) 372 (6), 237 (20), 190 (50), 189 (100).
The $^1H$ NMR (fig.**12**) showed four singlets (three for 3H each and one for 6H) between (δ in ppm.) 0.83 to 0.99 integrated for five tertiary methyl groups; two sharp singlets (3H each) that appeared at 2.03 and

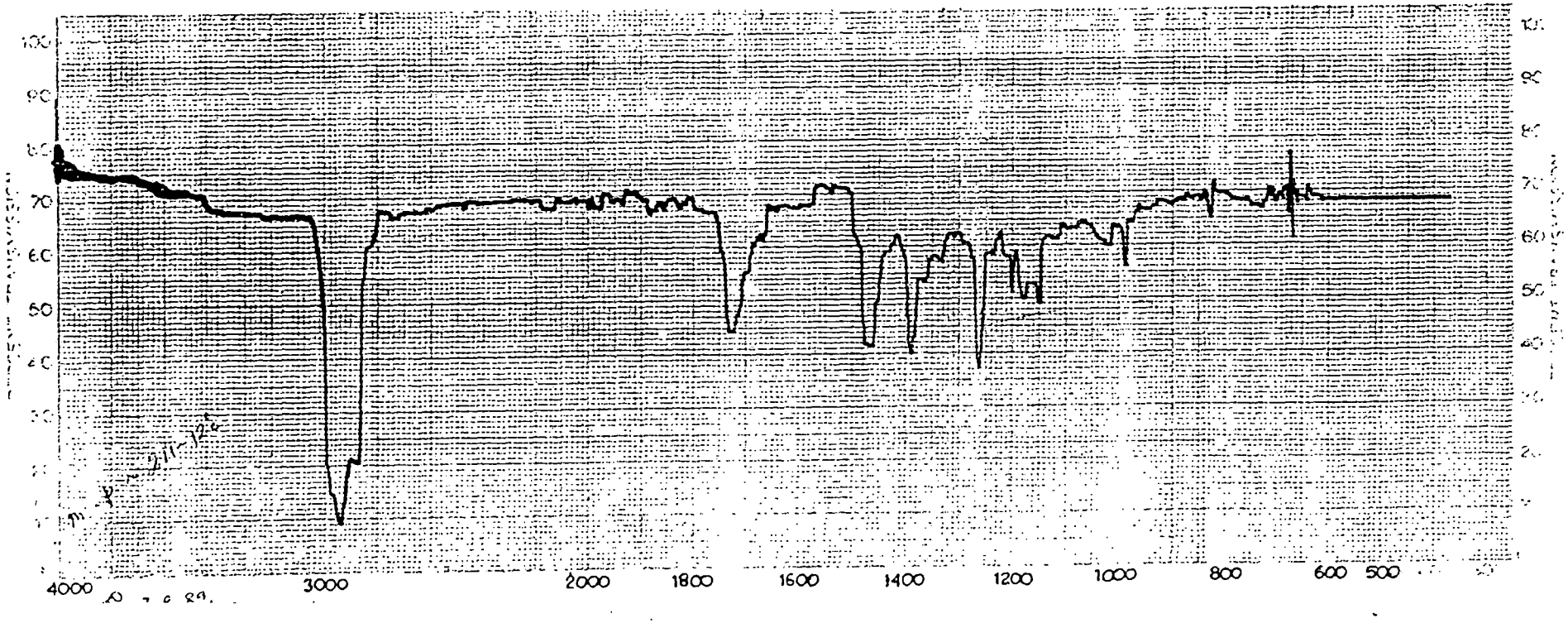



Fig.10, IR spectrum of 29-nor-acetyl,methyl,20-oxo, betulinate, 58.

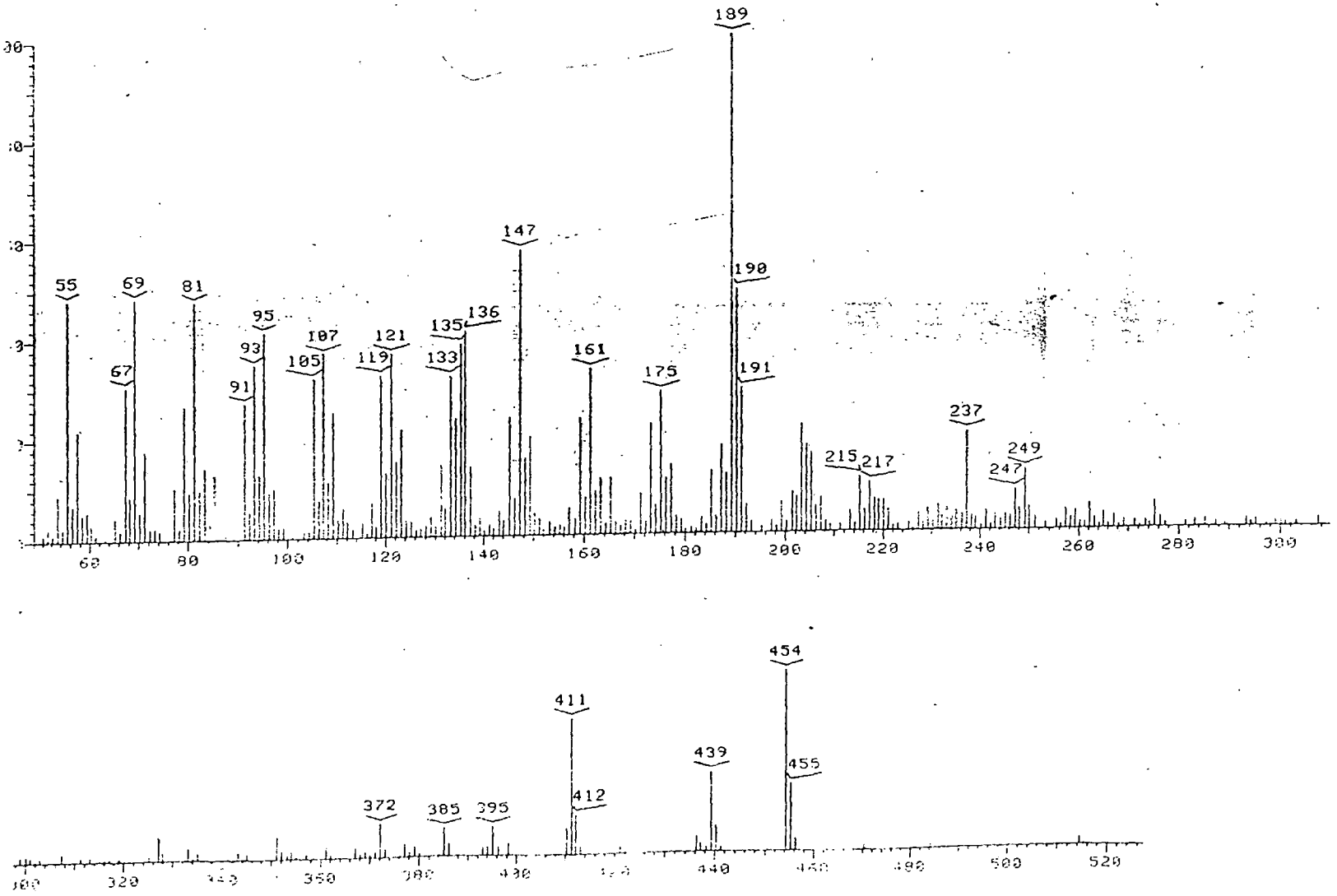



Fig.11, Mass spectrum of 29-nor-acetyl,methyl,20-oxo, betulinate, 58.

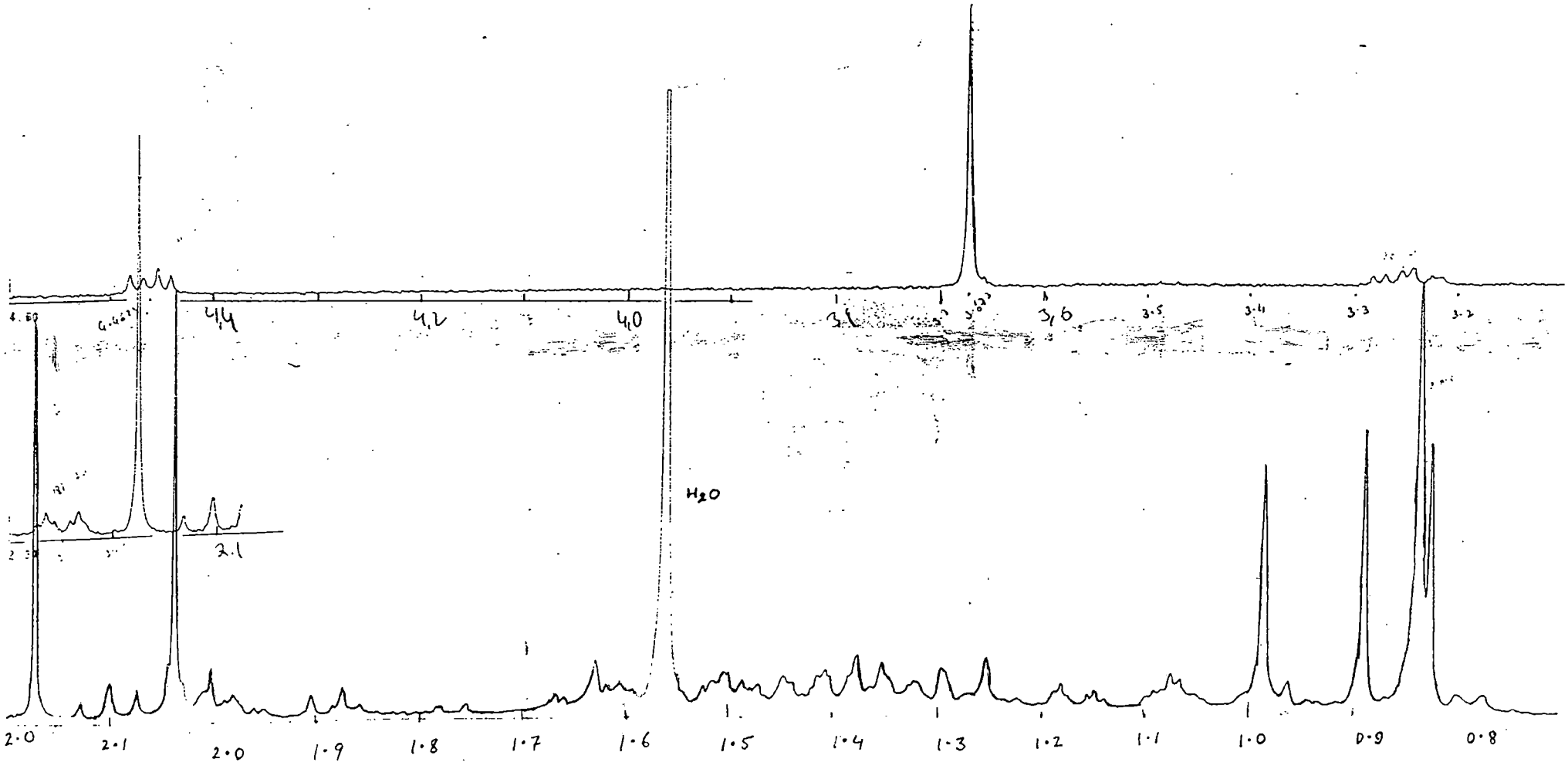



Fig.12, $^{1}H$ NMR spectrum of 29-nor-acetyl,methyl,20-oxo, betulinate, 58.

2.17 ppm are due to two acetyl groups one of which is at hydroxyl oxygen at C-3. The triplet of a doublet (1H) centred at 2.25 (J= 3 Hz) is probably due to the methine proton at C-18 ; the multiplet (1H) between 3.2 to 3.3 (ddd, J= 7 Hz) is accounted for a methine proton that coupled with neighbouring protons. The sharp singlet integrated for three protons at 3.67 is due to carbomethoxyl group at C-28 and the multiplet at 4.46 is accounted for the 3α-proton geminal to C-3 acetate group.

The absence of methylene protons and the C-30 methyl protons present in the starting compound **56** in which place the appearence of an additional $CH_3CO$ group with an α-proton to the acetyl group at 3.3 ppm as a multiplet suggest that the C-29 carbon is replaced by the oxygen atom to form the carbonyl group.

Thus,the structure of compound-D can be represented as 29-nor-acetyl-methyl 20-oxo-betulinate **58**.

Such type of compound (**57**) has been prepared by oxidation of betulin diacetate with hydrogen peroxide in acetic acid by Ruzicka et al[30].

Mechanism suggested :

The nature of formation of compound-C and D showed that the C-20-29 epoxide c undergoes epoxy ring cleavage in a different manner than those in the acid catalysed ones[27]. In this particular case the epoxide could breakup in two paths a and b to furnish products C and D.