ACTION OF N-BROMOSUCCINIMIDE ON FRIEDEL 3(4)-ENE IN DIMETHYL SULFOXIDE

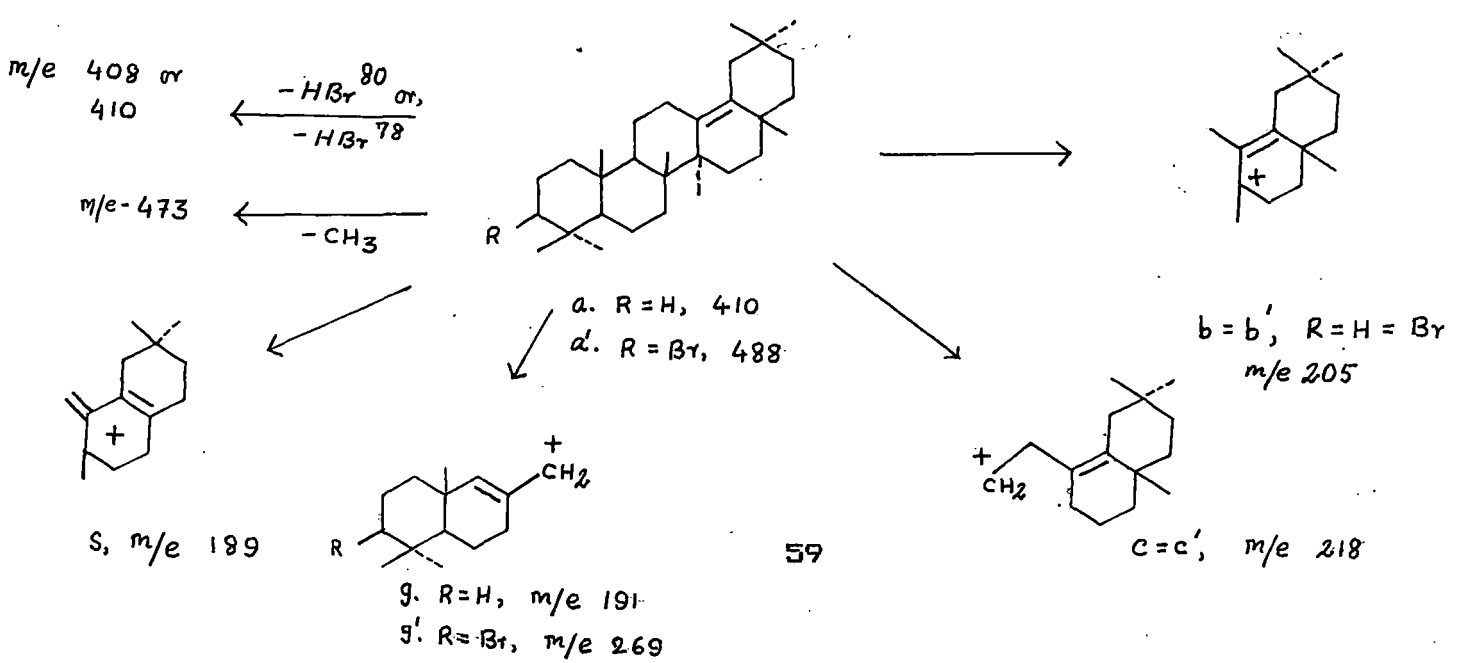
Friedel-3(4)-ene **54** was dissolved in small volume of chloroform and dimethyl sulfoxide was added followed by N-bromosuccinimide. The mixture was then kept in dark for 24 hours and the product obtained was chromatographed over silica gel column. On elution with solvents, two compounds A and B were separated with pet-ether and benzene-petrol (1:4) respectively.

Characterisation of compound A as 3α-bromo olean-13(18)-ene **55**.

The compound A was crystallised from chloroform-methanol mixture *M.P.*200-1°C; It gave positive Beilstein test for halogen and produced yellow colouration with tetranitromethane (TNM) showing the presence of a double bond.

The Mass spectrum (fig.1) showed the molecular ion peak m/e at 490 (M_1,36.5%, Br^{79})$^+$ and 488 (M_2,54%, Br^{77}); other important peaks appeared at 475 (M_1 -Me,50)$^+$, 473 (M_2 -Me,58)$^+$, 410 (M_1 -HBr^{79} and M_2-HBr^{77},12.5)$^+$; 408(6), 395(14), 274(8), 269(0.8), 257(10), 218(34), 205(40), 189(18), 109(80),95(100). The mass fragmentation pattern are in agreement with olean-13(18)-ene system[26] which is shown below in scheme-I.

SCHEME-I



Elemental analysis and mass suggests the molecular formula as $C_{30}H_{49}Br$

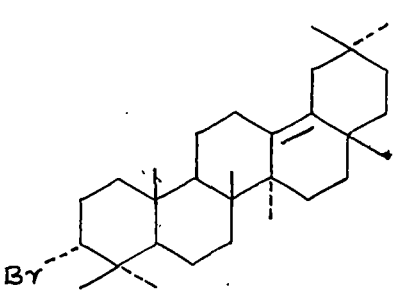
The ^1H NMR (fig.2) resonance signals are recorded in tabular form below :-

TABLE-I

Chemical shifts. (δ in ppm)	No.of protons.	Multiplicity.	Assignments.
0.79	3	singlet	
0.81	3	"	
0.83	3	"	8 tertiary
0.84	3	"	methyls.
0.86	3	"	
0.94	3	"	
1.08	6	"	
1.81	1	triplet of doublet. (J=3 & 13 Hz)	C_9-αH.
5.16	1	broad singlet (W 1/2 = 8 Hz.)	C_3-βH.

The triplet of a doublet centred at 1.81 ppm was due to α-proton at C-9 coupled with neighbouring methylene protons and the broad singlet at 5.15 ppm for β-proton at C-3.

Hence from the spectral data the compound A was isolated as 3α-bromo olean-13(18)-ene **55**.



55,

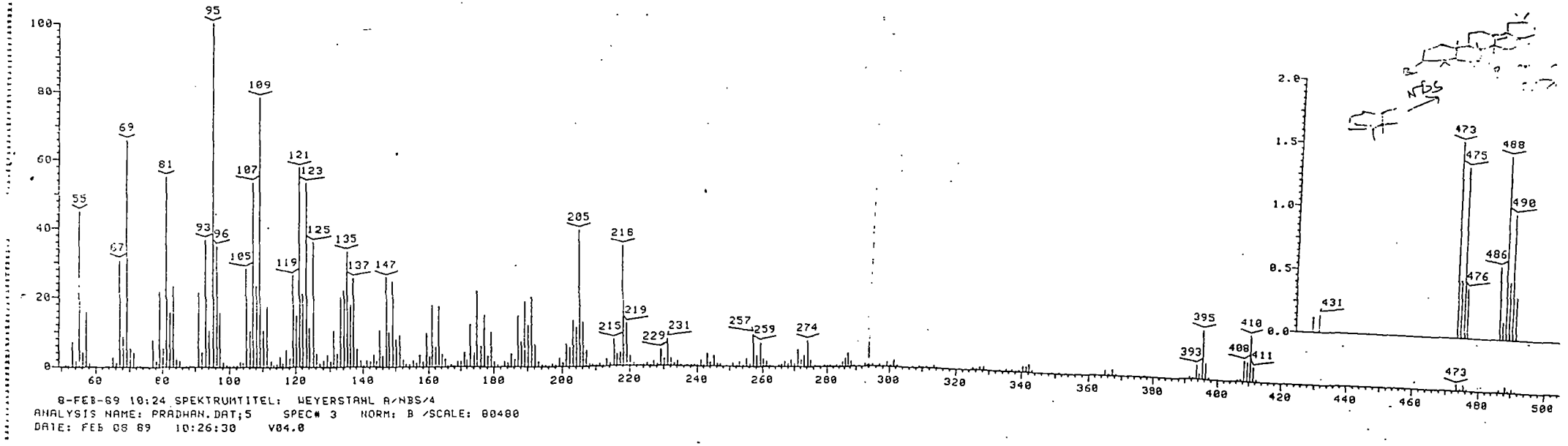


Fig.1. Mass spectrum of 3α- bromo-olean-13(18)-ene, 55.

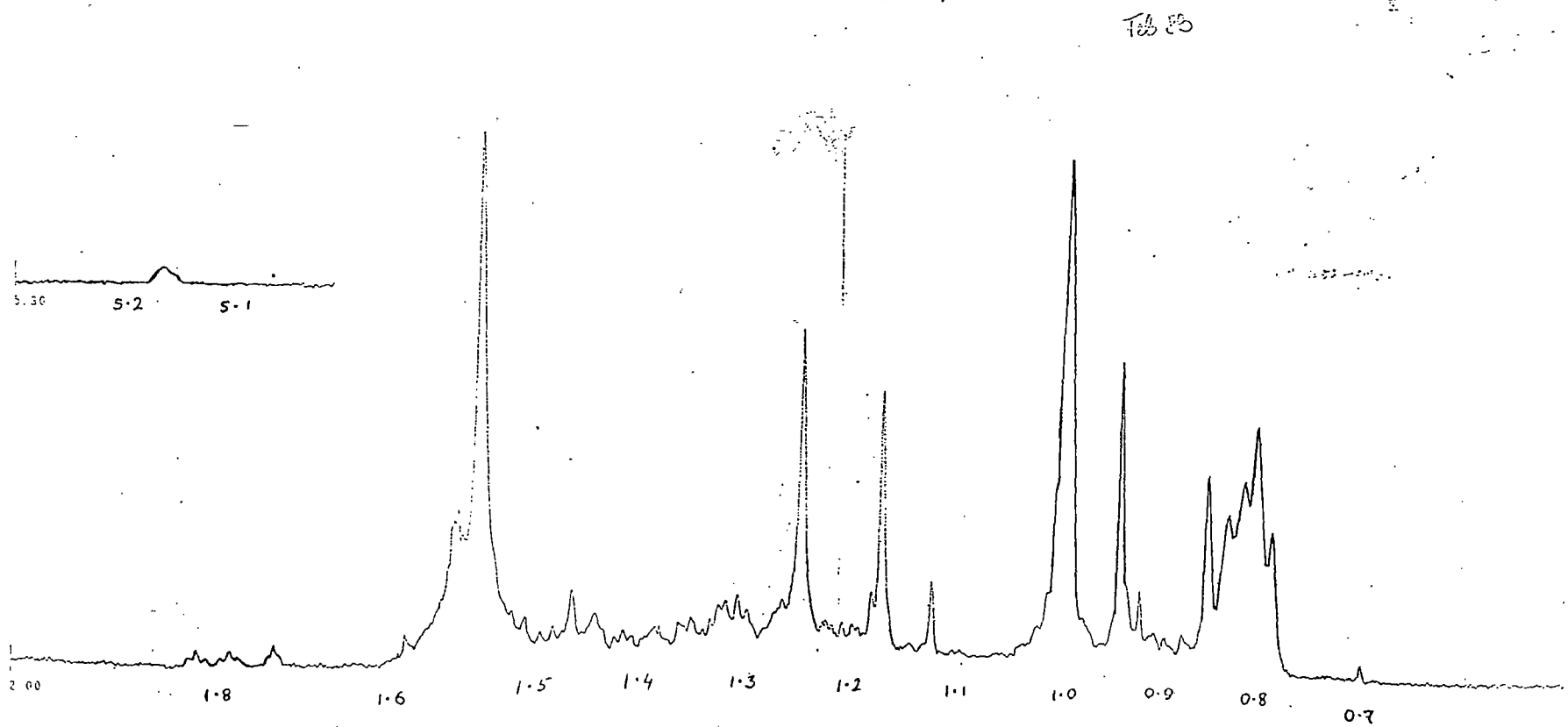
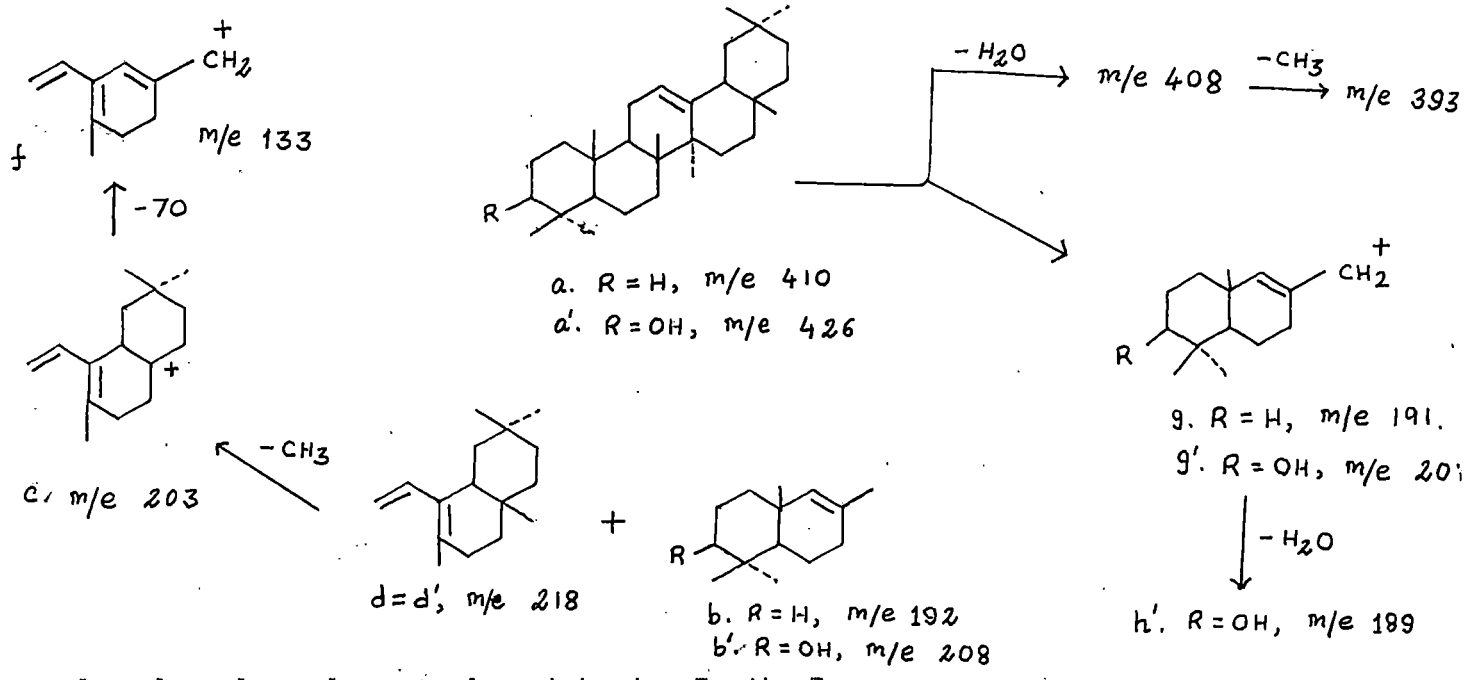


Fig.2. ^{1}H NMR spectrum of 3α- bromo-olean-13(18)-ene, 55.

Characterisation of compound B as 3β-hydroxy olean-12(13)-ene 56.

The compound B was crystallised from chloroform-methanol, M.P.229-30°C It gave yellow colouration with TNM but did not respond to Beilstein test for halogen. IR spectrum (fig.3) showed absorption peak at 3380 cm^{-1} for hydroxy group. Mass spectrum (fig.4) gave molecular ion peak at m/e 411 (M -Me,18)$^+$, 408(M -18,27), 395(10),393(17),255(29),229(24), 218(20),207(4),205(40),203(18),189(18),173(34),145(46),133(36),125(76) 95 (100). The fragmentation pattern are in agreement with that type suggested for olean-12(13)-ene by Djerassi et al[26] as given below in scheme-II.

SCHEME-II



Its molecular formula was found to be $C_{30}H_{50}O$.

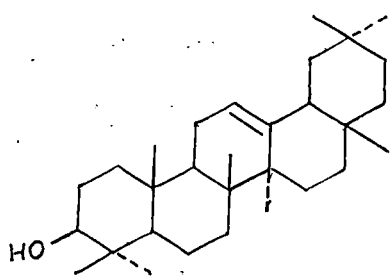
The ^1H NMR (fig.5) signals are recorded below in table-II.

TABLE-II

Chemical shifts. (δ in ppm)	No.of protons.	Multiplicity.	Assignments.
0.79	3	singlet	
0.81	3	"	

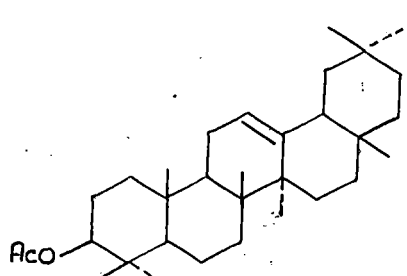
0.82	3	"	8 tertiary
0.87	3	"	methyls.
0.94	3	"	
0.99	3	"	
1.06	6	"	
4.08	1	broad singlet like.	equatorial methine proton.
5.53	1	triplet (J= 3 & 7 Hz)	olefinic proton.

The broad singlet at 4.08 ppm is due to α-proton at C-3 coupled with neighbouring protons and triplet at 5.53 ppm for olefinic proton at C-12. Hence, ^{1}H NMR suggested the structure for compound B as 3β-hydroxy olean-12(13)-ene **56a**.



56a,

This was confirmed by preparation of its derivative **56b** with pyridine-acetic anhydride. The acetate so prepared had the molecular formula $C_{32}H_{52}O_2$, *M.P.*234-5°C, IR : 1690 and 1255 cm^{-1}, was identical with an authentic sample of β-amyrin acetate **56b**.



56b,

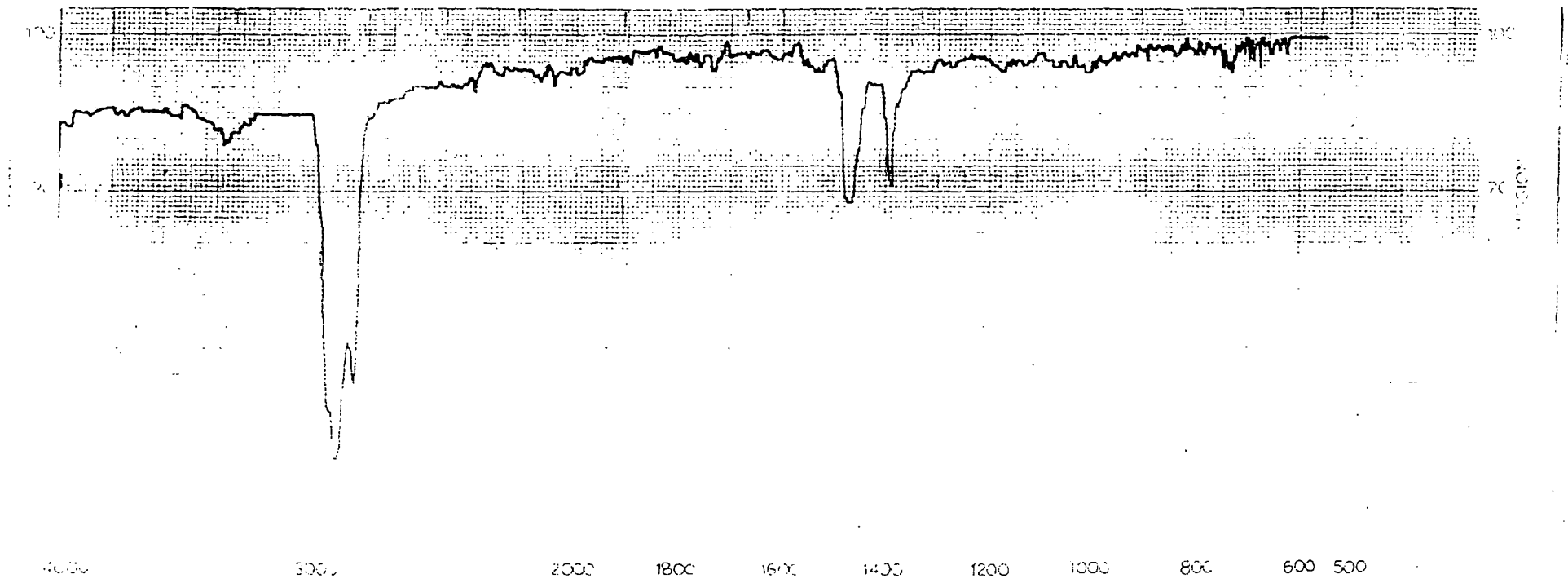


Fig.3. IR spectrum of 3β-hydroxy-olean-12(13)-ene, 56a.

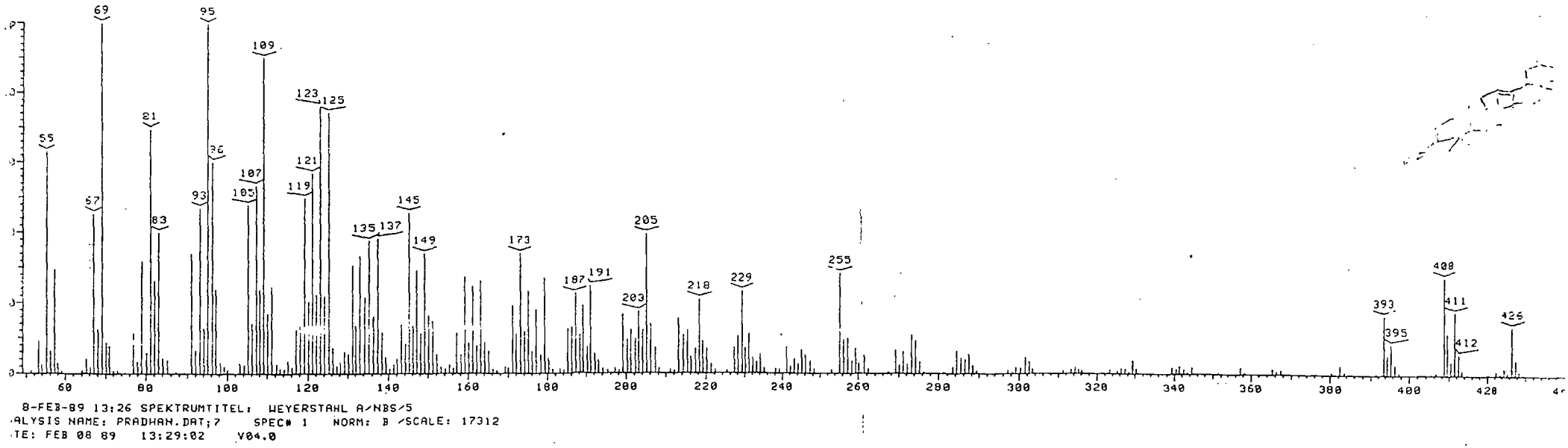


Fig.4. Mass spectrum of 3β-hydroxy-olean-12(13)-ene, 56a.

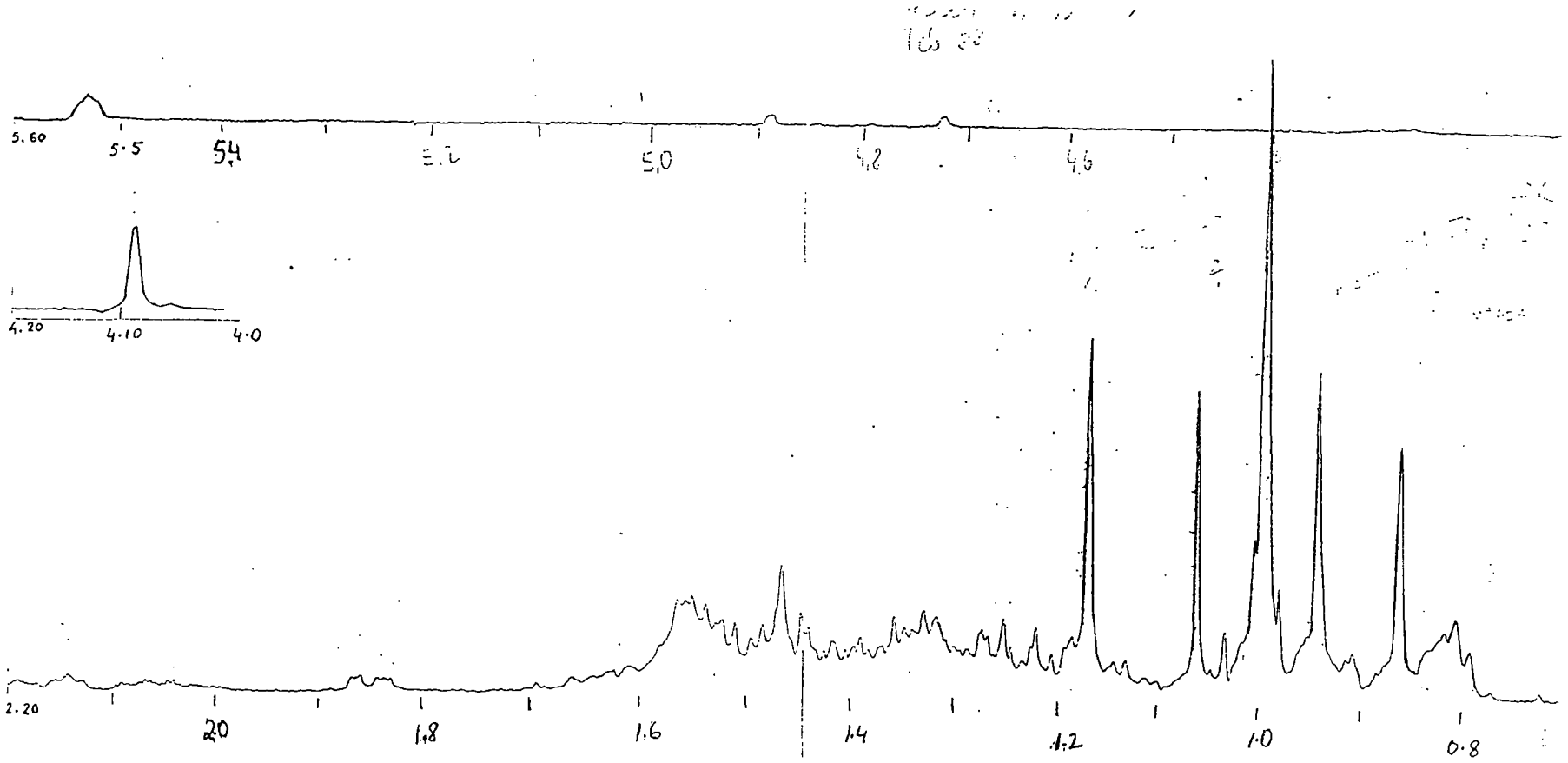
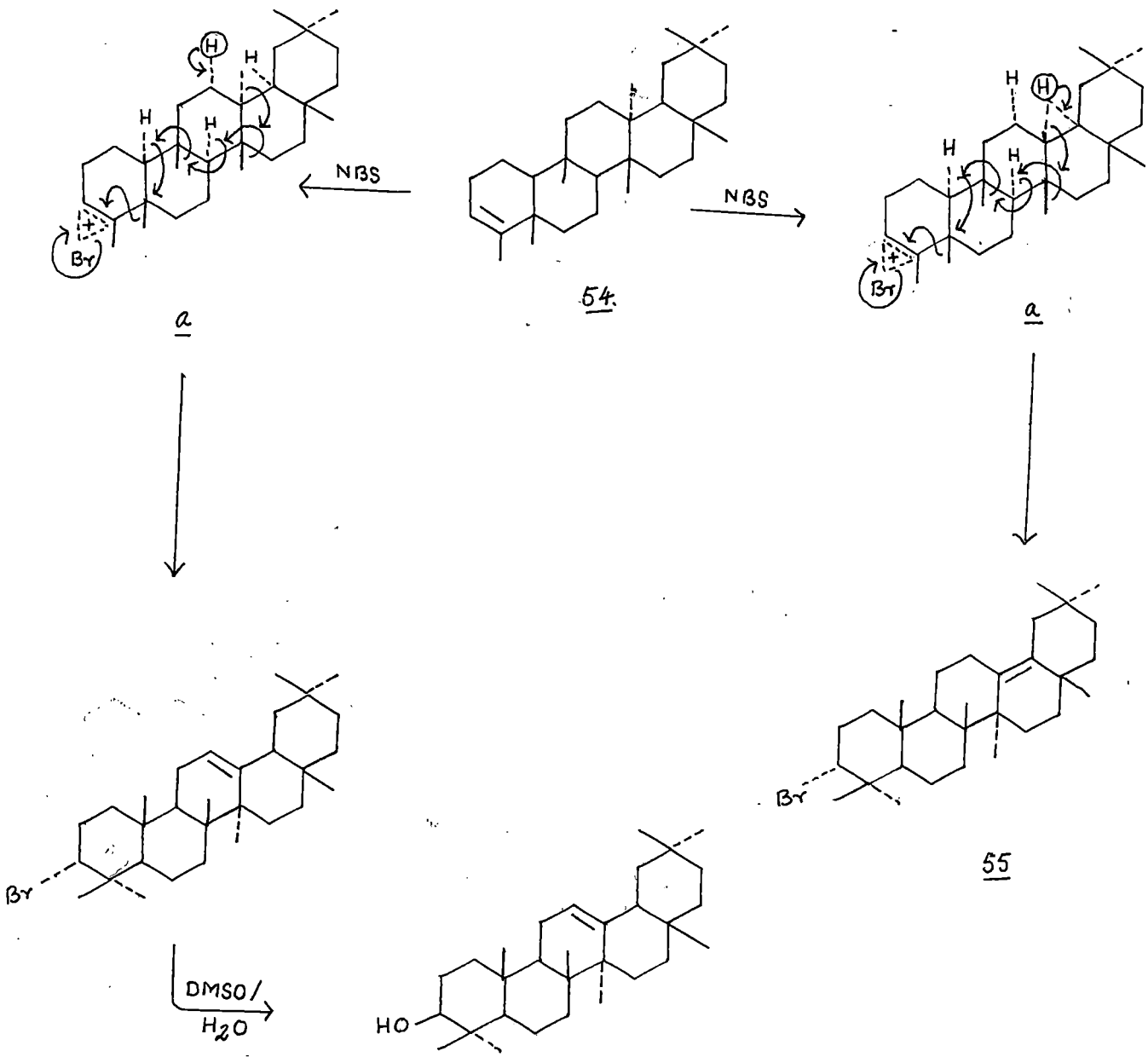


Fig.5. ^{1}H NMR spectrum of 3β-hydroxy-olean-12(13)-ene, 56a.

Mechanism proposed :-

It is not surprising to note the formation of olean-13(18)-ene and olean-12(13)-ene derivative from friedel-3(4)-ene in this reaction. The attack of the bromonium ion from the rare side gives the cation a which opens up either to form a carbonium ion at C-4 or it undergoes concerted backbone rearrangement[276] either to form the olean-13(18)-ene derivatives 55 or olean-12(13)-ene derivative 56a



54

a

a

55

56a

ACTION OF BROMINE ON LUPENYL ACETATE IN ACETIC ACID.

Lupenyl acetate **57a**, which was prepared from Lupeol **57**, (see Experimental), was dissolved in acetic acid cooled at 0^{o}-5^{o}C and bromine was added. After 30 minitues it was worked up in a usual way and the product obtained was subjected to chromatography. On elution with petrol a solid material,compound-D,was obtained.

Characterisation of compond-D :- Isolation of 3β-acetyl 19α,29,30 tribromo Oleanane.

Compound-D was crystallised from chloroform-methanol, M.P. 225-26^{o}C; It responded strongly to Beilstein test for halogen but did not produce yellow colouration with TNM indicating absence of double bond. IR spectrum (fig.6) showed absorption peaks at 1690 and 1255 cm^{-1} showing the presence of acetate group. Mass spectrum (fig.7) analysis showed molecular ion peak at m/e 710 $(M,0.2\%)^{+}$, with other important peaks appearing at 708 (0.5), 706 (0.8) 648 (1.5) 646 (1.5) 626 (2) 566 (2) 533 (2.8) 466 (2.8), 189 (30), 82 (96), 80 (100).

Elemental analysis showed the molecular formula of compound-D is $C_{32}H_{51}O_2Br_3$.

Its ^{1}H NMR spectrum (fig.8) resonance signals are recorded below in table-III.

TABLE-III.

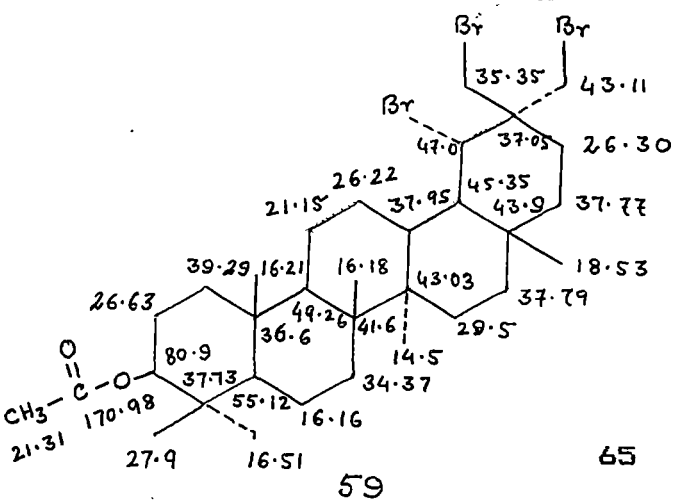
Chemical shift (δ in ppm)	No. of proton	Multiplicity	Assignment.
0.84	3	singlet	
0.85	3	"	
0.86	3	"	

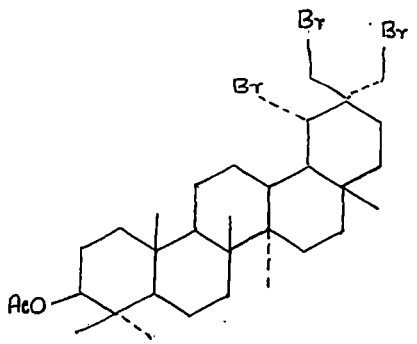
0.94	3	"	6X t-CH_3
0.95	3	"	
1.06	3	"	
2.05	3	singlet	$-OCOCH_3$
3.5-3.9	2	AB_q (J=10 Hz)	$-CH_2Br$
3.8-4.6	2	AB_q (J=11.5 Hz)	$-CH_2Br$
4.48	1	multiplet	$-C_3-\alpha H$.
4.24	1	doublet	$-C_{19}-\beta H$.

.....

The ^1H NMR spectral data clearly indicated that there are only six tertiary methyl groups. The C-29 methylene and the C-30 methyl on the C_{20-29} olefinic double bond have disappeared and in these positions two AB quartets for a pair of CH_2-X groupings have appeared. Since from elemental and MS spectral analysis the existance of three bromine atoms have been indicated in compound-D, these groupings must be present as two $-CH_2Br$ groupings. The third proton that came in existance is a doublet at 4.24 ppm with coupling constant of 12 Hz showing that the third bromine is in secondary carbon that has an axial neighbouring proton, indicating that the bromine is equatorially oriented with a geminal axial proton that coupled with the neighbouring axial proton giving rise to large J value of 12 Hz.

The ^{13}C NMR spectrum (fig.9) also accounts for 32-carbon atoms. Chemical shifts (in ppm) of each carbon atom are shown below within the structure proposed 59 for compound-D.





59

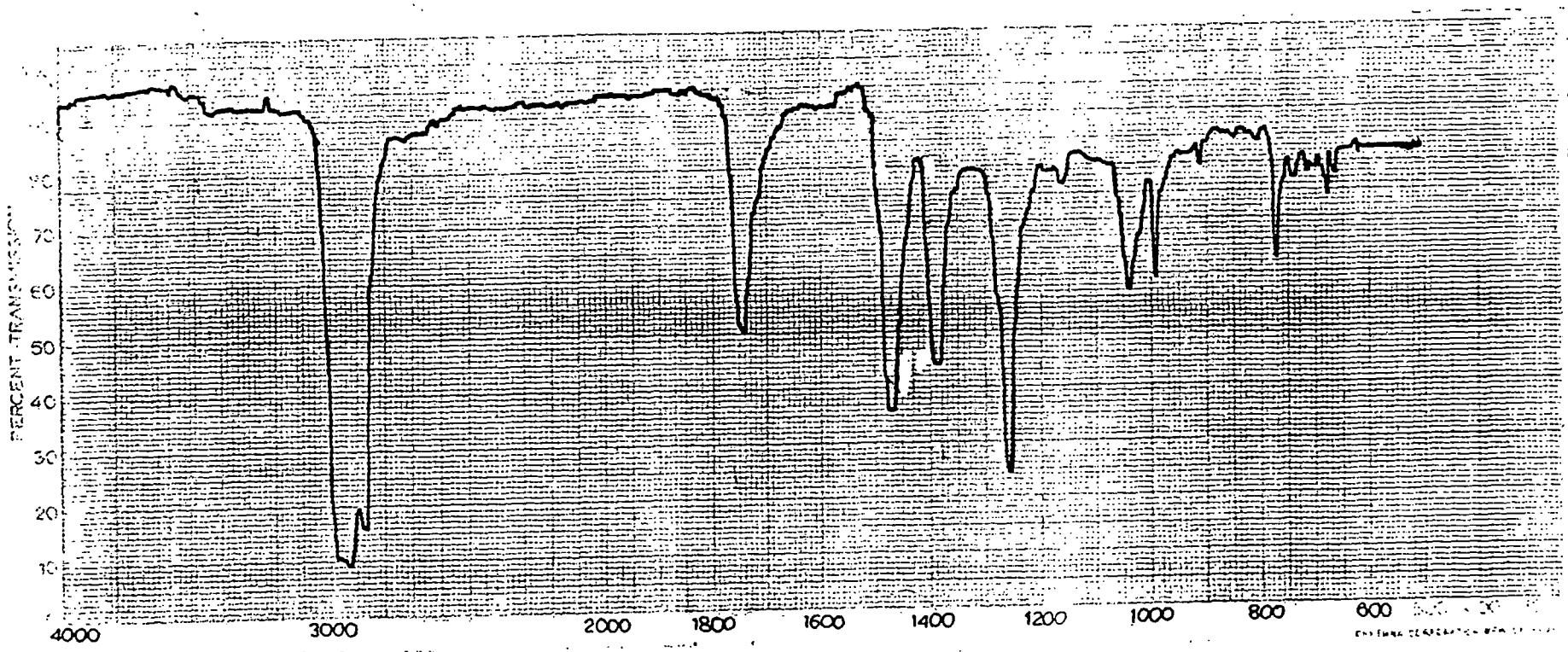


Fig. 6, IR spectrum of 3β-acetyl 19α,29,30 tribromo Oleanane, 59.

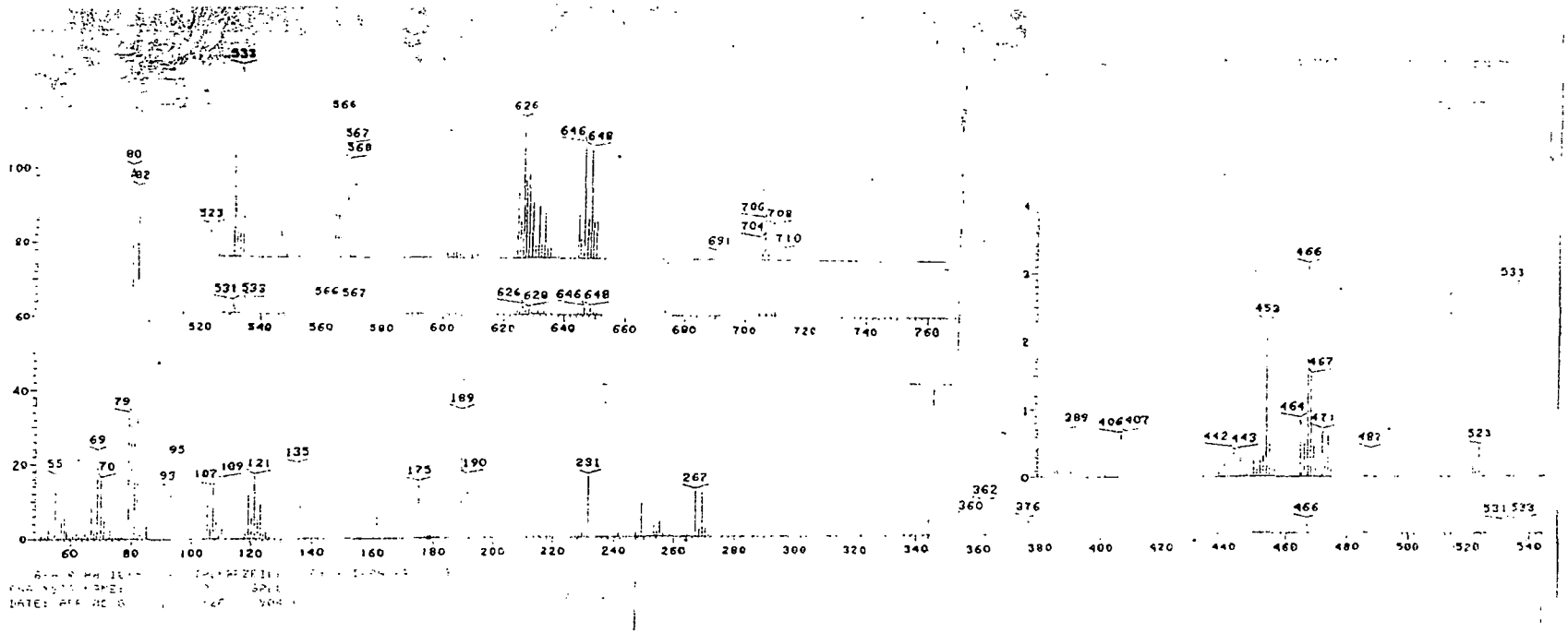


Fig. 7, Mass spectrum of 3β-acetyl 19α,29,30 tribromo Oleanane, 59.

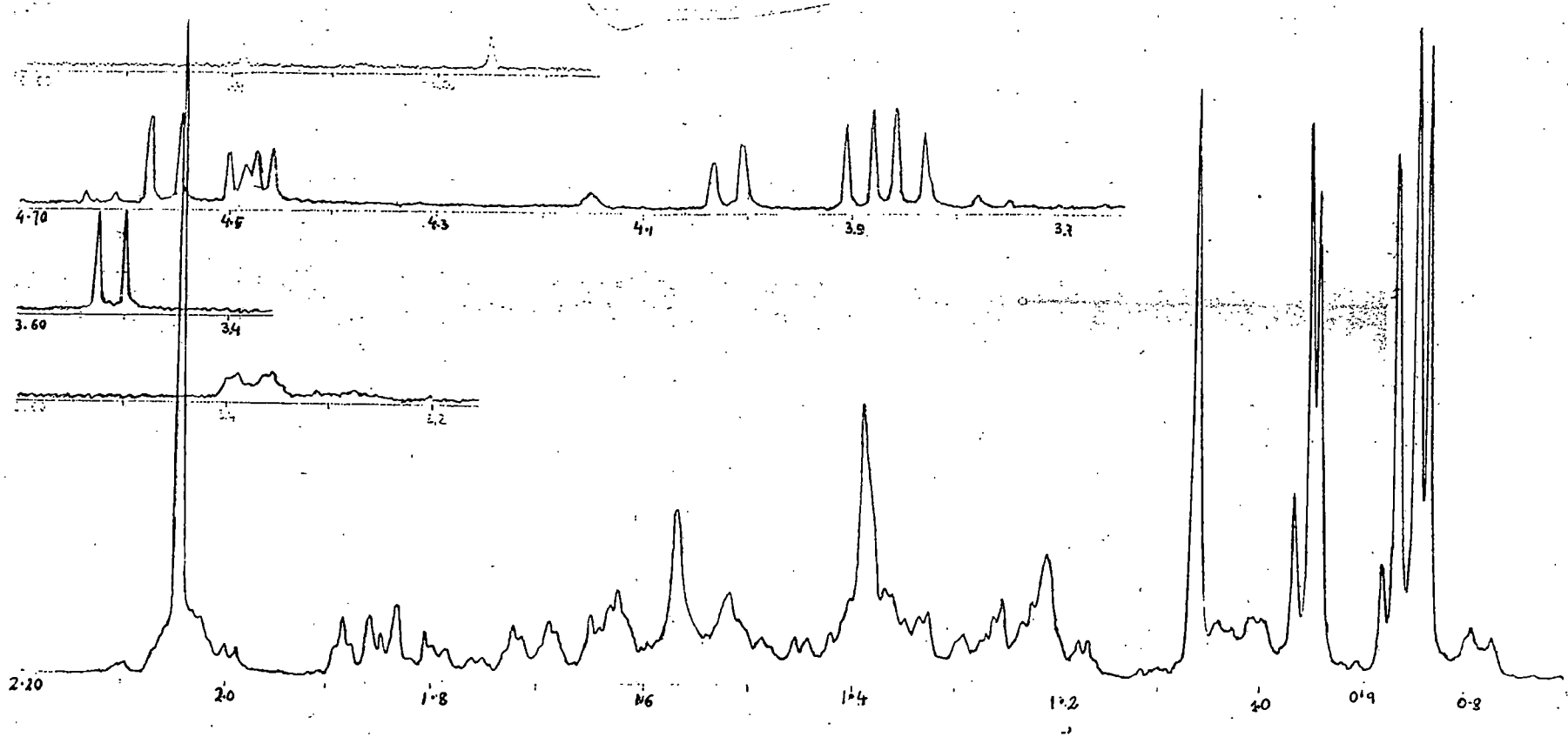


Fig. 8, ^{1}H NMR spectrum of 3β-acetyl 19α,29,30 tribromo Oleanane, 59.

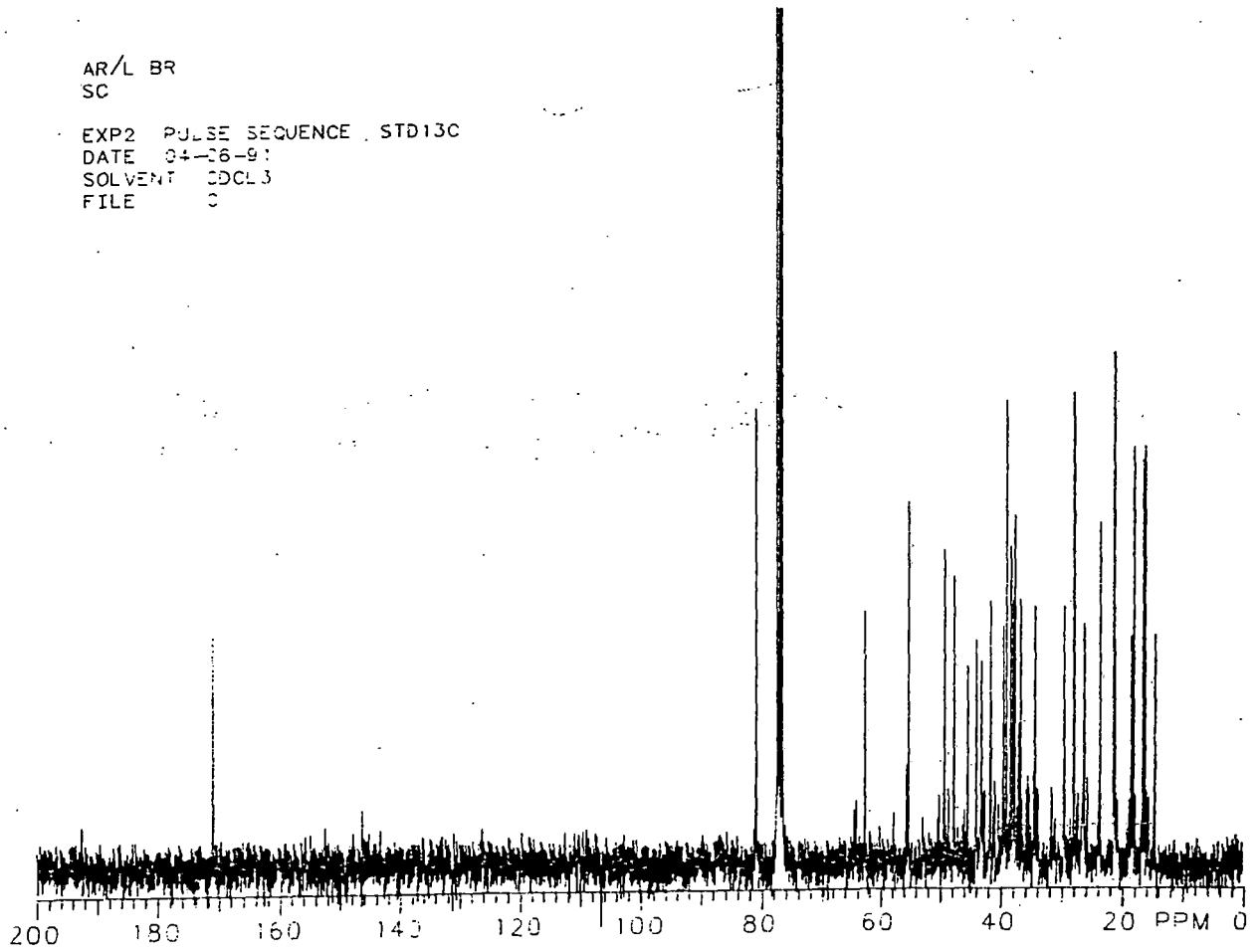


Fig. 9, ^{13}C NMR spectrum of 3β-acetyl 19α,29,30 tribromo Oleanane, 59.

Pradhan et al[10,20] have demonstrated that acetyl methyl betulinate **47**/ lupenyl acetate **57a** on treatment with N-bromosuccinimide in dimethyl -sulfoxide gave 3β-acetyl 29,30-dibromo-olean 28→19β-olide **49** / 3β-acetyl 29,30-dibromo-oleanan-18αH,19α-ol respectively.

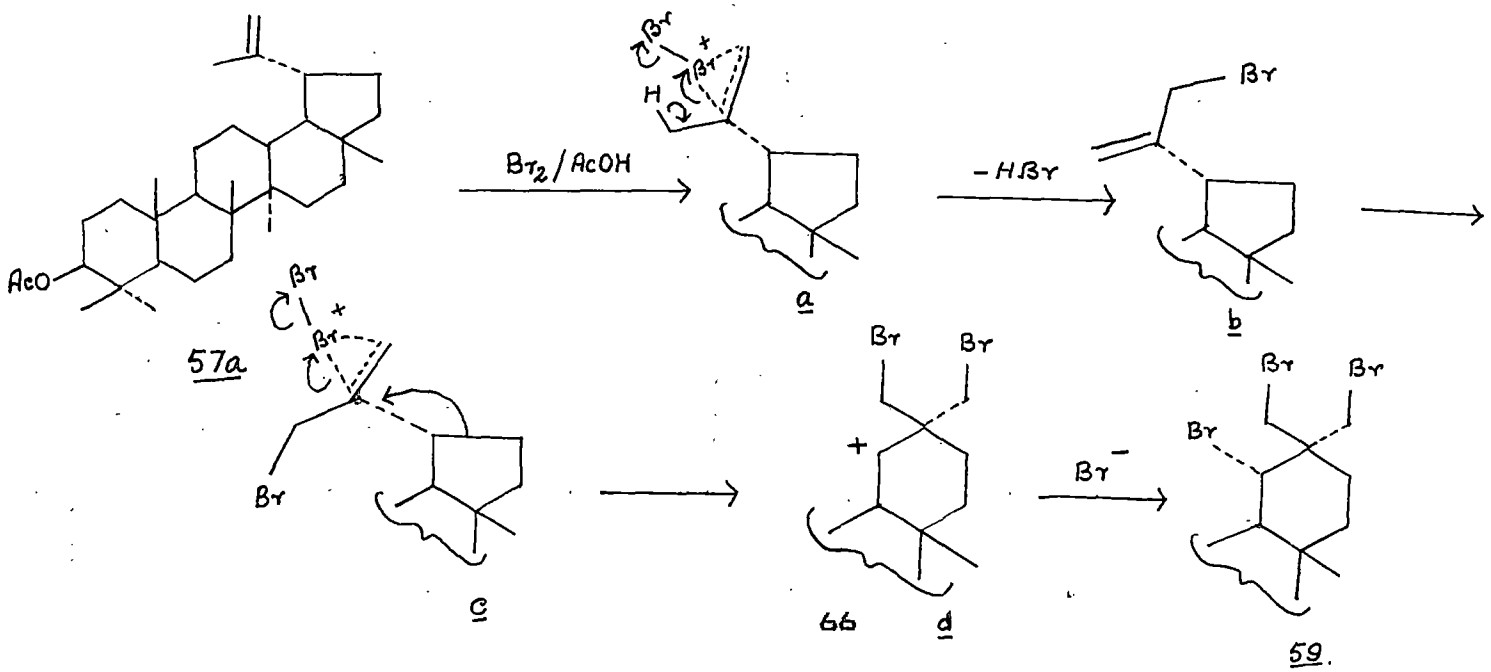
Assuming that the reaction with bromine in acetic acid on lupenyl acetate also proceed by almost the same mechanism the product-D may be assigned the structure **59**, which clearly explains the spectral data observed so far.

In order to establish the mechanism, 30-bromo-lupenyl acetate **58** (prepared from lupenyl acetate, see Experimental) was brominated with bromine in acetic acid method and the product obtained, was found to be identical with 3β-acetyl 19α,29,30 tribromo oleanane **59**.

Mechanism :-

The molecular bromine probably attacks the olefinic double bond to form the cation **a** which rearranges to form the allylic bromo compound **b**. The allylic bromo compound undergoes bromonium ion attack to give the cation **c** which undergoes ring expansion as in the previous cases[18,20] to furnish the cation **d**. The cation accepts the bromide ion from the rare side to furnish the sterically favoured tri-bromo compound.

Thus, the structure of compound D was established to be 3β-acetyl 19α,29,30 tribromo oleanane **59**. The same compound was prepared from lupenyl acetate as reported[25] without giving details of its structure and mechanism.



ACTION OF N-BROMOSUCCINIMIDE ON LUPAN 20(29)-EN 3β,28-DIOL IN DIMETHYL SULFOXIDE.

Lupan 20(29)-en-3β,28-diol (Betulin) **60** was dissolved in minimum volume of chloroform and dimethyl sulfoxide was added followed by N-bromosuccinimide. It was than kept in dark and the reaction product thus obtained was chromatographed. On elution with petrol,a crystall--ine compound-E was obtained.

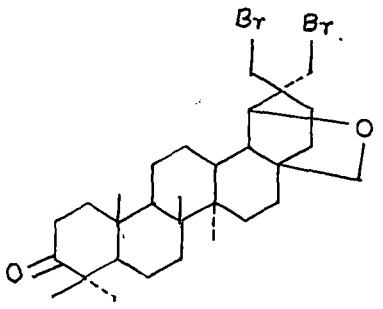
Characterisation of compound-E : Isolation of 3-keto olean 28-19-oxo-29,30-dibromide.

The compound-E was crystallised from chloroform-methanol, *M.P.*232-3°C; it responded to Beilstein test for halogen but did not gave yellow colouration with TNM indicating the absence of double bond. IR spectrum (fig.**10**) showed absorption peak at 1720 cm^{-1} for the presence of carbonyl group. Mass spectrum (fig.**11**) showed molecular ion peak at m/e 599 (M_1^+,Br^{79}, 2%),along with other important peaks were at 597 (M_2^+,Br^{77},6),519 (M-HBr^{79},14)$^+$, 517(M-HBr^{77},18)$^+$, 483(6), 439(10), 423(6), 407(8), 293(8), 283(10), 267(10), 189(40), 109(70), 95(70), 81 (88), 55 (100).

Elemental analysis showed presence of two bromine atoms and molecular formula $C_{30}H_{46}O_2Br_2$.

The ^1H NMR spectrum (fig.**12**) showed five singlets integrated for three protons each at (δ in ppm) 0.93, 1.03, 1.10, 1.14 and 1.21 indicating five tertiary methyl groups; a multiplet centred at 2.68 was accounted for methylene protons at C-2; one AB quartet with coupling constant value 5 Hz at 3.69 was due to coupling between two geminal protons at C-28, while two other AB quartets that appeared in the region 3.50-3.71 (J=8 Hz) and 3.59-3.82 (J=10 Hz) ppm each integrated for two protons were probably due to two $-CH_2Br$ groups at C-29 and C-30 of the rearranged ring-E. The doublet at 3.98 ppm (J=3 Hz) may be accounted for the methine proton at C-19.

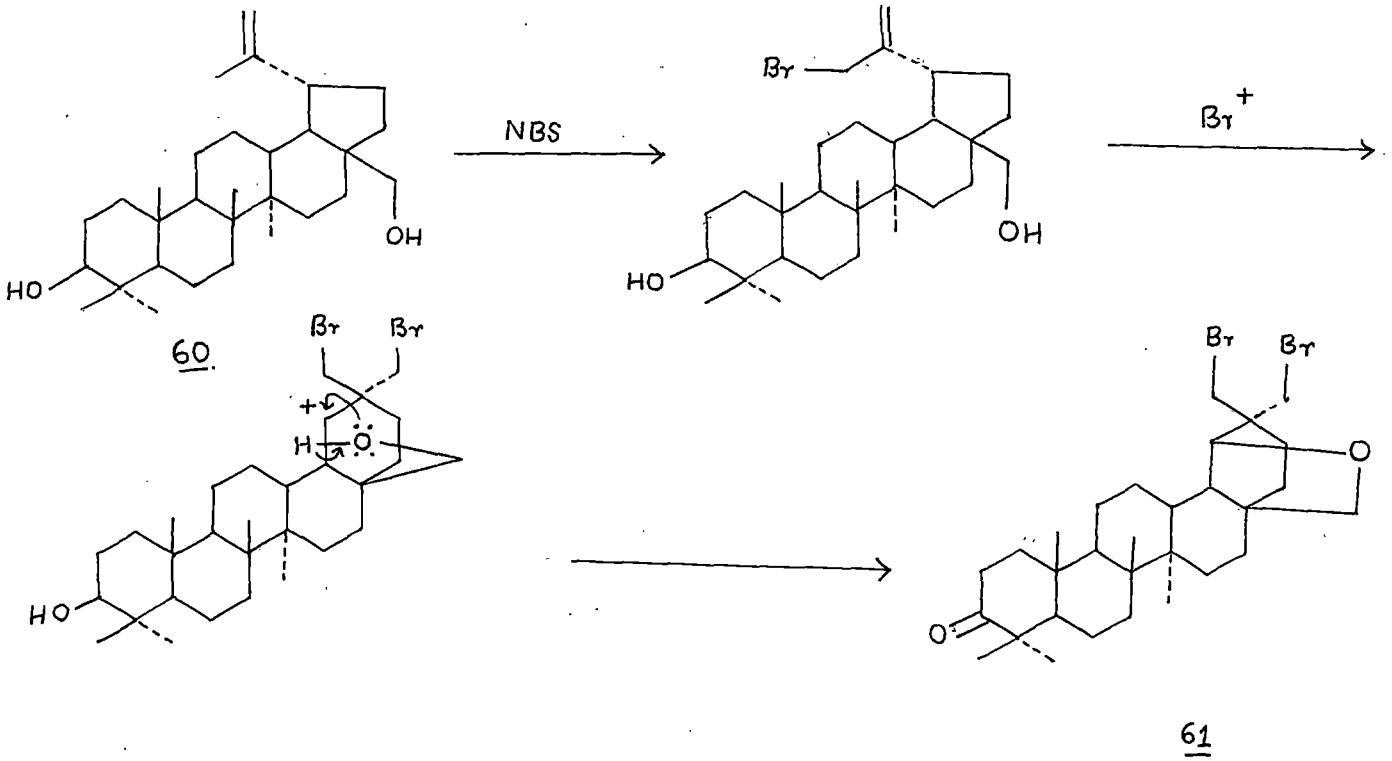
Hence compound-E was identified as 3-keto olean 28-19-oxo 29,30 dibromide 61 from the above spectral analysis.



61

Mechanism proposed :-

The E-ring enlargement by N-bromosuccinimide has been reported[18,20] earlier from our laboratory. In this case also bromonium ion attacks the double bond thereby causing ring enlargement along with cyclic ether formation at C-28 while the hydroxy group at C-3 was oxidised to carbonyl group.



61

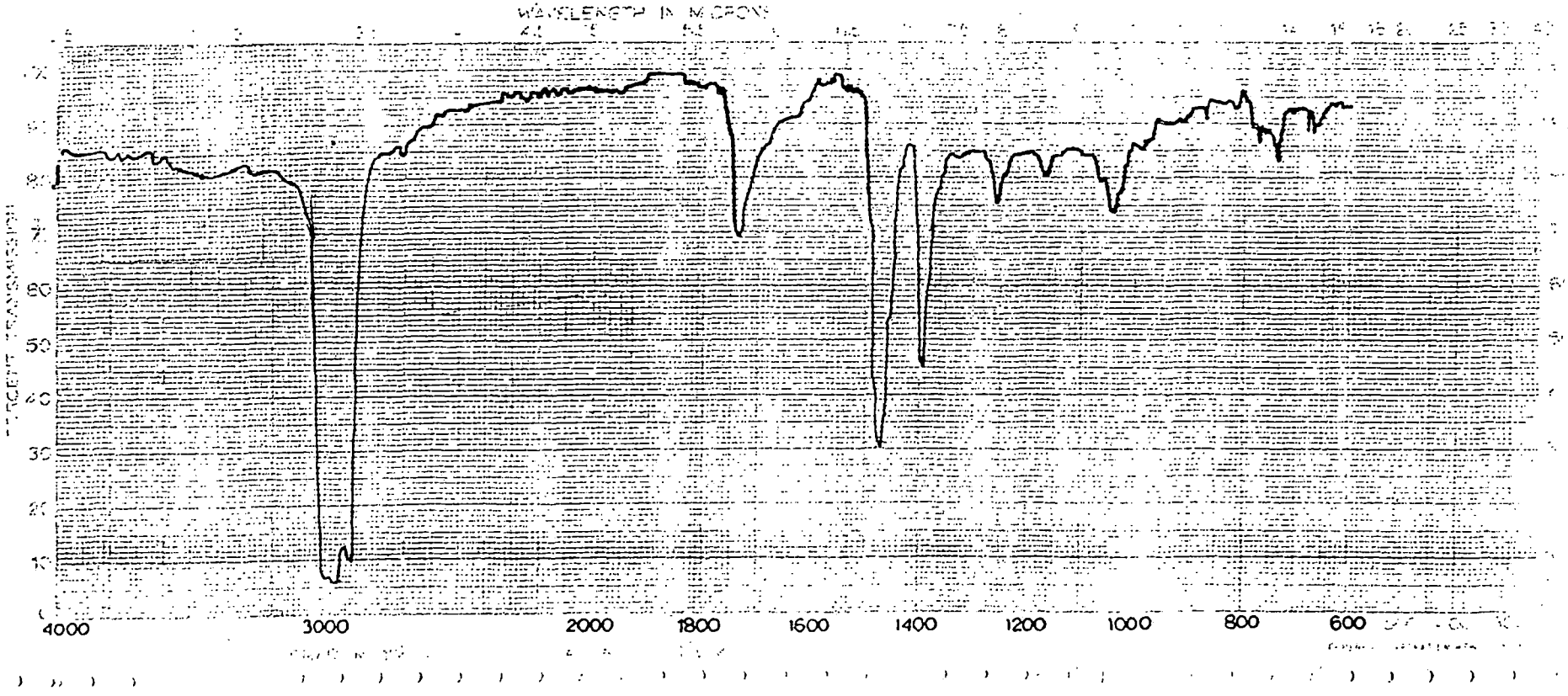


Fig. 10, IR spectrum of 3-keto Olean 28-19-oxo 29,30 dibromide, 61.

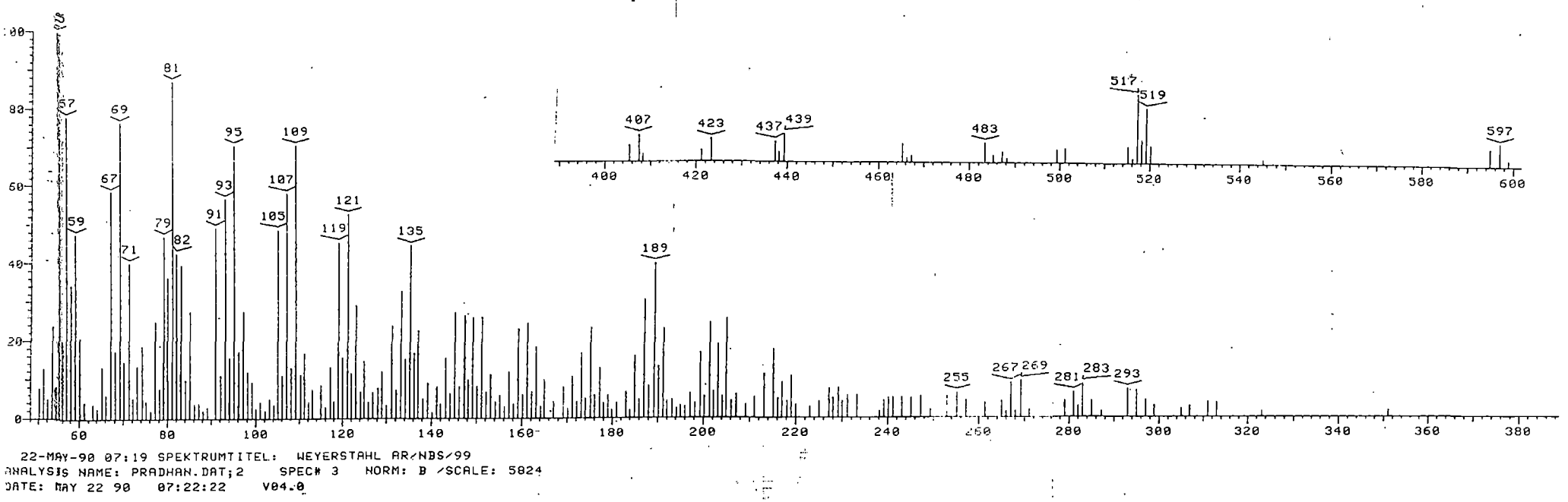


Fig. 11, Mass spectrum of 3-keto-Olean 28-19-oxo 29,30 dibromide, 61.

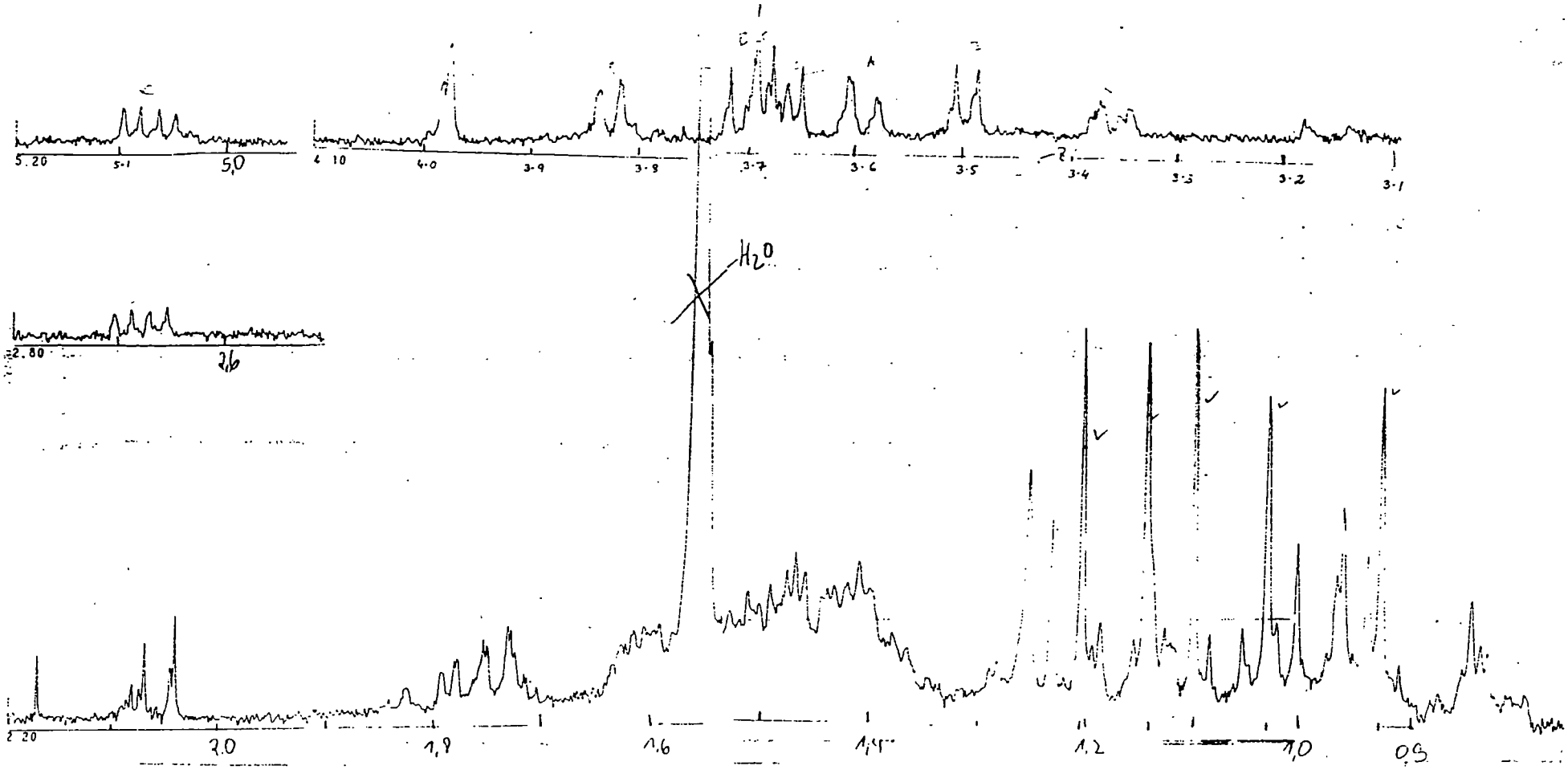


Fig. 12. ^{1}H NMR spectrum of 3-keto Olean 28-19-oxo 29,30 dibromide, 61.

ACTION OF N-BROMOSUCCINIMIDE ON LUP-20(29)-EN-3β,28-DIYL ACETATE IN DIMETHYL SULFOXIDE.

Lup-20(29)-en-3β,28-diyl acetate 62 was dissolved in chloroform containing dimethyl sulfoxide and N-bromosuccinimide was added. It was than kept in dark for 24 hours and the gummy product obtained after workup was subjected to chromatography, which on elution two compounds F and G were obtained with benzene-petrol (3:2) and benzene respectively.

Identification of compount-F :-

Compound-F was crystallised from chloroform-methanol, *M.P.* 169-70°C; It responded to Beilstein test for halogen and gave yellow colouration with TNM. IR spectrum (fig. **13**) showed absorption peaks at 1240 and 1730 cm^{-1} indicating the presence of acetate carbonyl group. Mass spectrum (fig. **14**) showed molecular ion m/e at 606(M_1^+,Br^{79},1.8), while other fragments appeared at 604(M_2^+,Br^{77}1.9),593 (0.4),592 (0.9), 577 (0.3), 546 (24), 531 (20),511 (18),466 (45),465 (60),451 (60),405 (36),267 ,201,189 (100). Its molecular fomula was calculated to be $C_{34}H_{53}O_4Br$.

The ^1H NMR spectrum (fig.**15**) resonance signals are recorded below in tabular form :-

TABLE-IV

Chemical Shift (δ in ppm)	No. of Proton	Multiplicity	Assignment.
0.83	3	singlet	
0.85	3	"	
0.98	3	"	5 X t-CH_3
1.05	3	"	
1.26	3	"	
2.03	3	singlet	2 X -$COCH_3$
2.07	3	"	

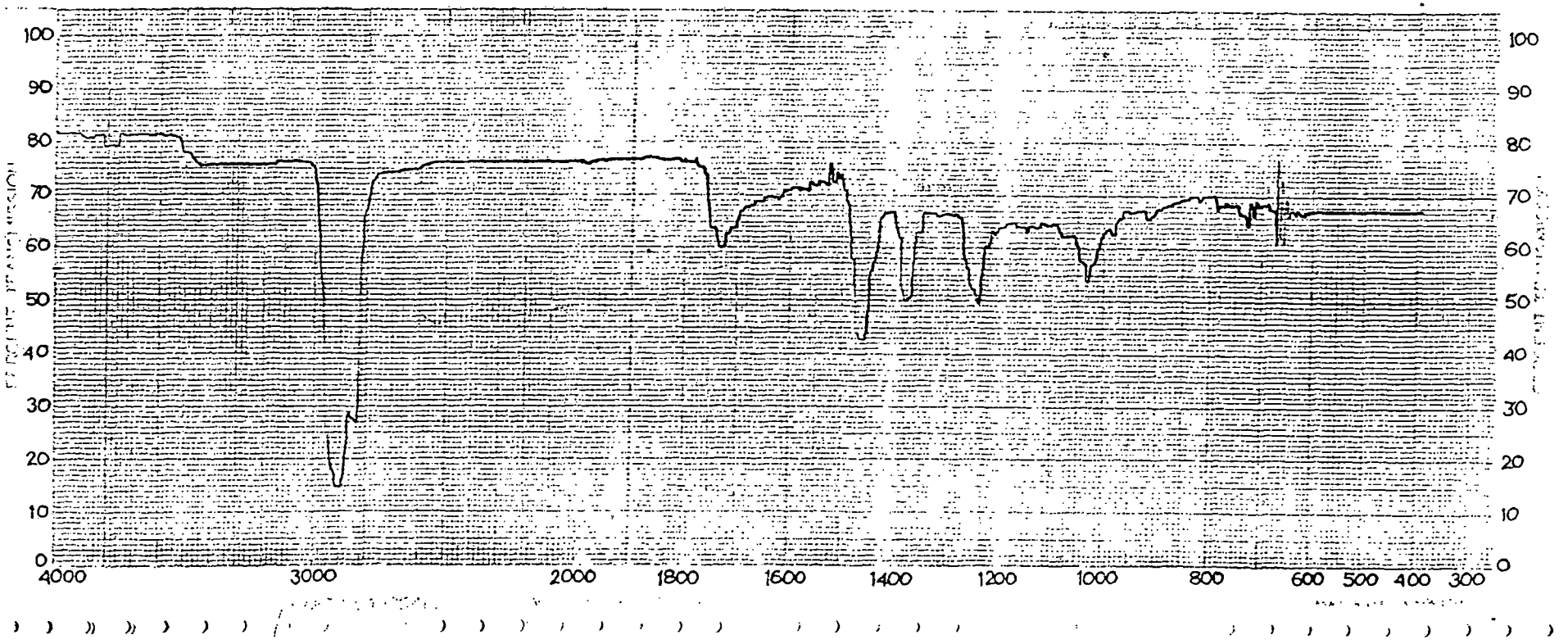


Fig. 13, IR spectrum of 30-bromo Lup-20(29)-ene 3β,28-diyl acetate, 63.

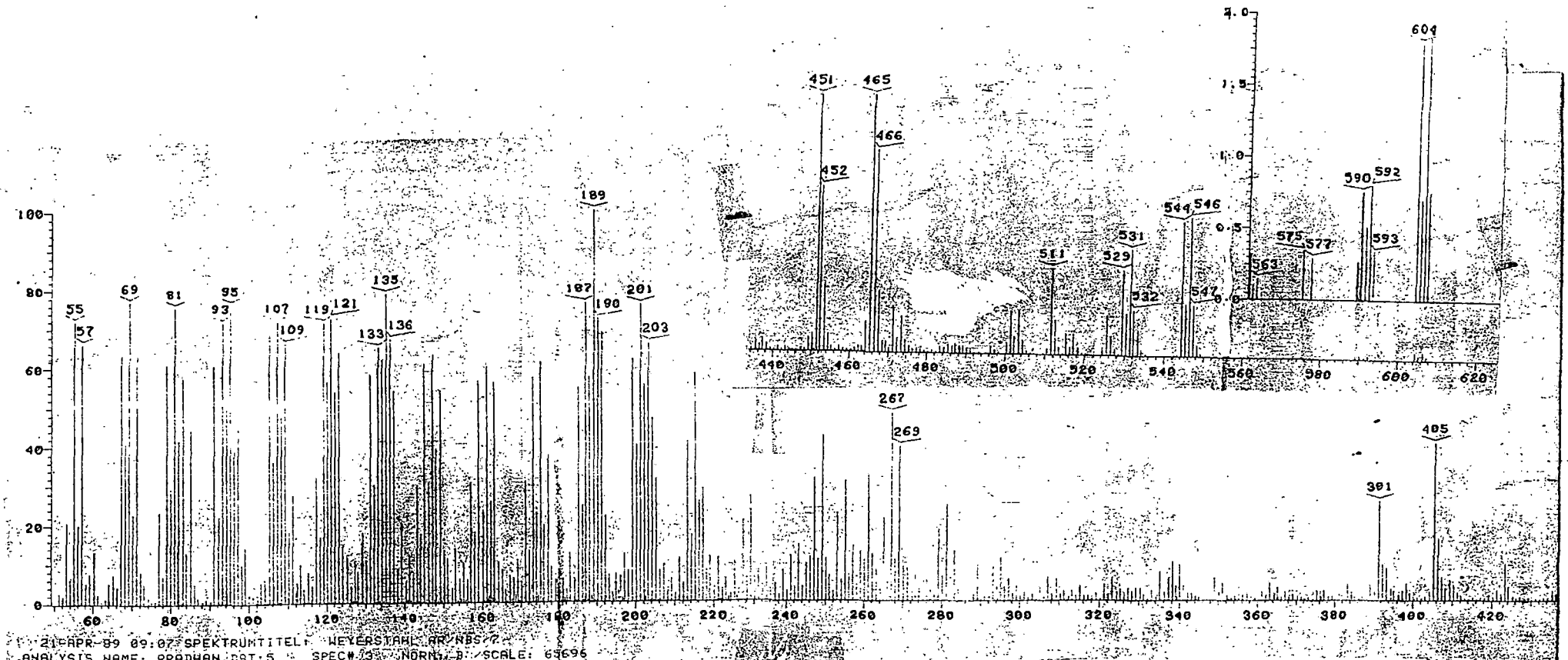


Fig. 14, Mass spectrum of 30-bromo Lup-20(29)-ene 3β,28-diyl acetate, 63.

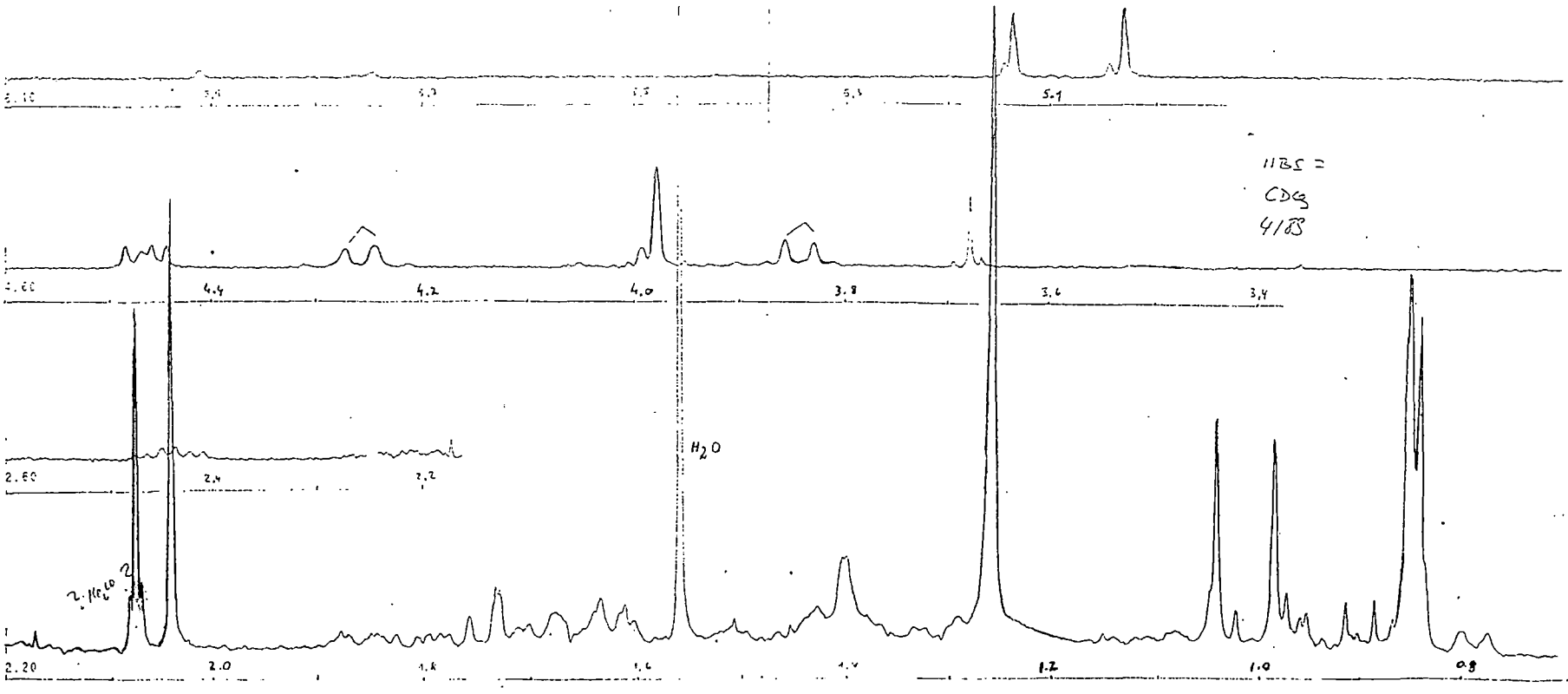
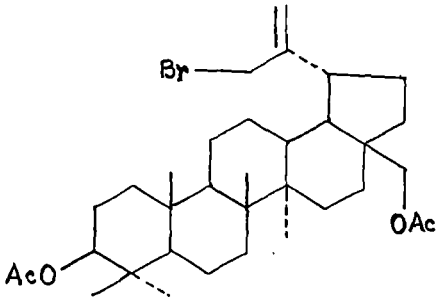


Fig. 15, ^{1}H NMR spectrum of 30 bromo Lup-20(29)-ene 3β,28-diyl acetate, 63.

3.91	2	singlet	$-CH_2OAc$.
3.84	1	doublet	$-CH_2Br$.
4.26	1	"	
4.47	1	multiplet	$C_3\alpha$-H
5.03			
5.12	2	2 X singlet	$C=CH_2$

The increase of 78 and 80 mass units in the molecular weight of the starting material 62 shows that only one bromine atom is introduced in the compound F. The appearance of a pair of doublet at 3.84 and 4.26 ppm with J value of 11 Hz are due to the methylene proton geminal to the bromine, the other signals being almost similar to that of the starting material 62.

Thus compound F can be designated as 30-bromo betulin diacetate or 30-bromo-lup-20(29)-en-3β,28-diyl acetate 63.



63

Identification of compound-G :-

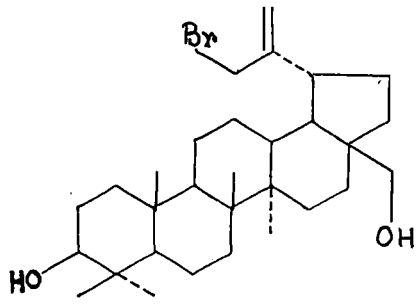
The compound G was crystallised from cloroform-methanol, *M.P.*202-3^{o}C; It gave yellow colouration with TNM showing the presence of double bond and responded to Beilstein test for halogen. IR spectrum (fig.16) showed broad absorption peak at 3390 cm^{-1} indicating the presence of hydroxy group while there was no absorption in the carbonyl region showing the absence of acetate group. Mass spectrum showed molecular ion peak at 442. Its molecular formula is calculated to be $C_{30}H_{50}O_2Br$ from elemental analysis and mass.

The ^1H NMR spectrum (fig.17) showed five singlets at

(δ in ppm) 0.76,0.82,0.96,0.98 and 1.02 due to five tertiary methyl groups; a multiplet centred at 3.19 was due to $C_3\alpha$-H coupled with neighbouring protons at C-2; the double doublets at 3.15 (J=10 Hz) and 3.78 (J=10 Hz) were due to two protons attached to carbon atom C-30 bearing the bromine atom; a broad singlet at 4.12 was due to two protons of C-28 containing the hydroxy group. Finally the two singlets at 4.9 and 4.95 appeared for the two olefinic protons at C-29.

In the Mass spectrum (fig.**18**) of compound G showed the maximum ion peak at m/e 442 shows that there is loss of HBr from the parent molecule G. The other fragments appeared at m/e 440(10), 425(10), 409(18), 369(25), 207(24), 189(46), 135(68), 107(76), 91(74)..

Thus from the above spectral analysis the compound G was designated as 30-bromo 3β,28-dihydroxy-lup-20(29)-ene **64**



64

It may be concluded that in the case of 28-O-acetate no bromination on the olifinic double bond at C-20(29) takes place whereas in other cases (lupenyl acetate[20] and lupan-20(29)-ene 3β,28-diol **60**,section-C) both allylic bromination and bromination on the double bond accompanied by ring enlargement occurs to furnish oleanane skeleton.

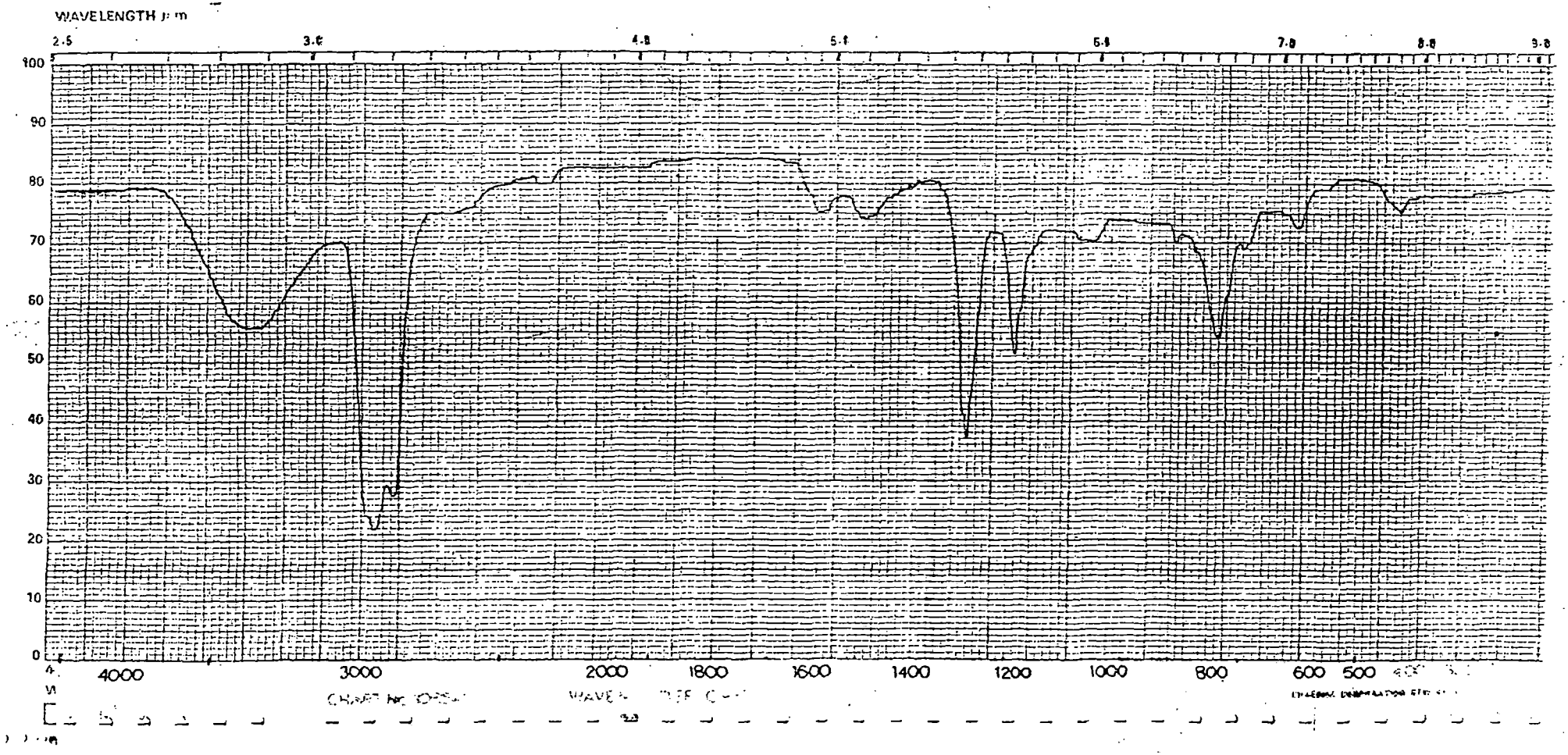


Fig. 16, IR spectrum of 30-bromo Lup-20(29)-ene 3β,28-diol, 64.

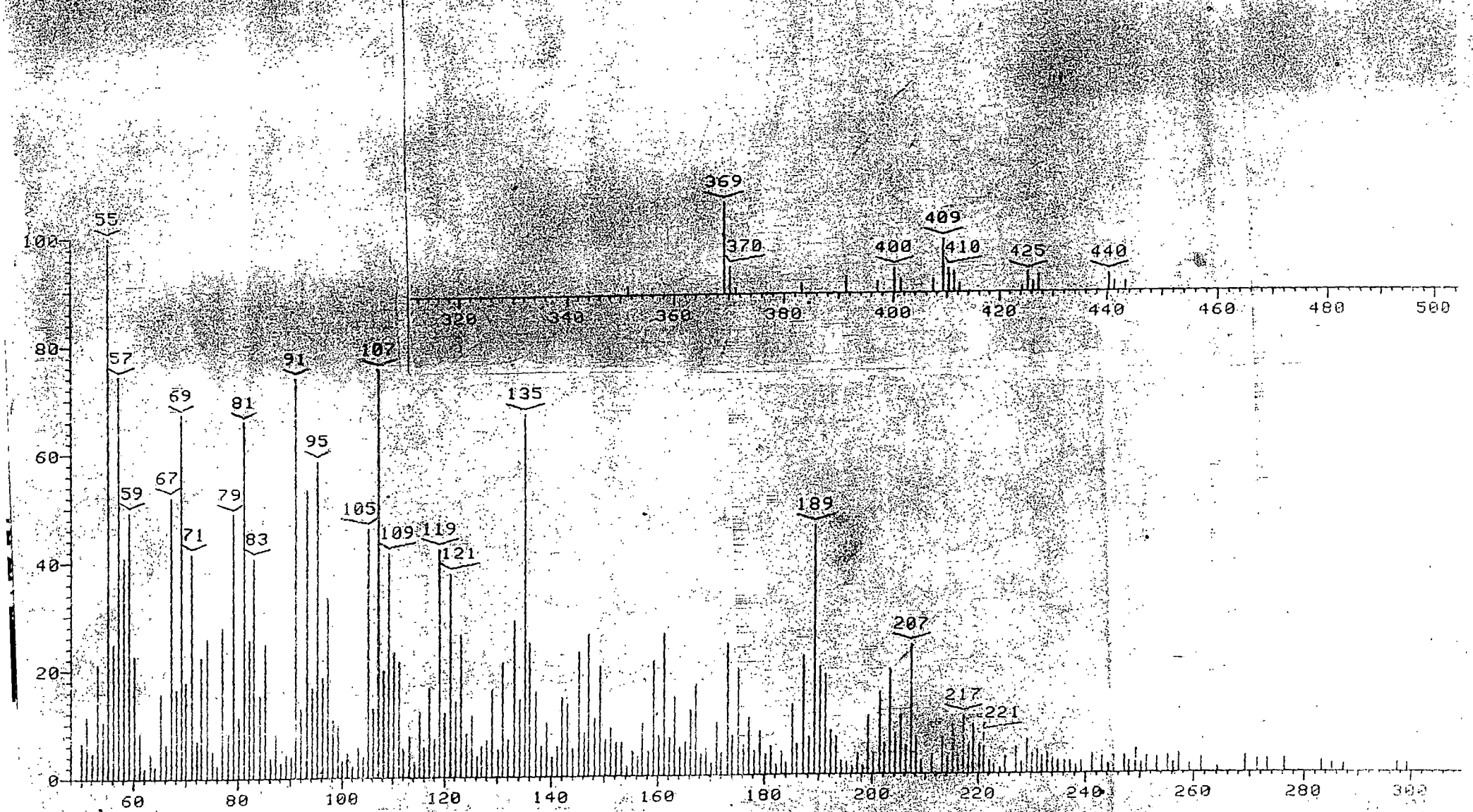


Fig. 17. Mass spectrum of 30-bromo Lup-20(29)-ene 3β,28-diol, 64.

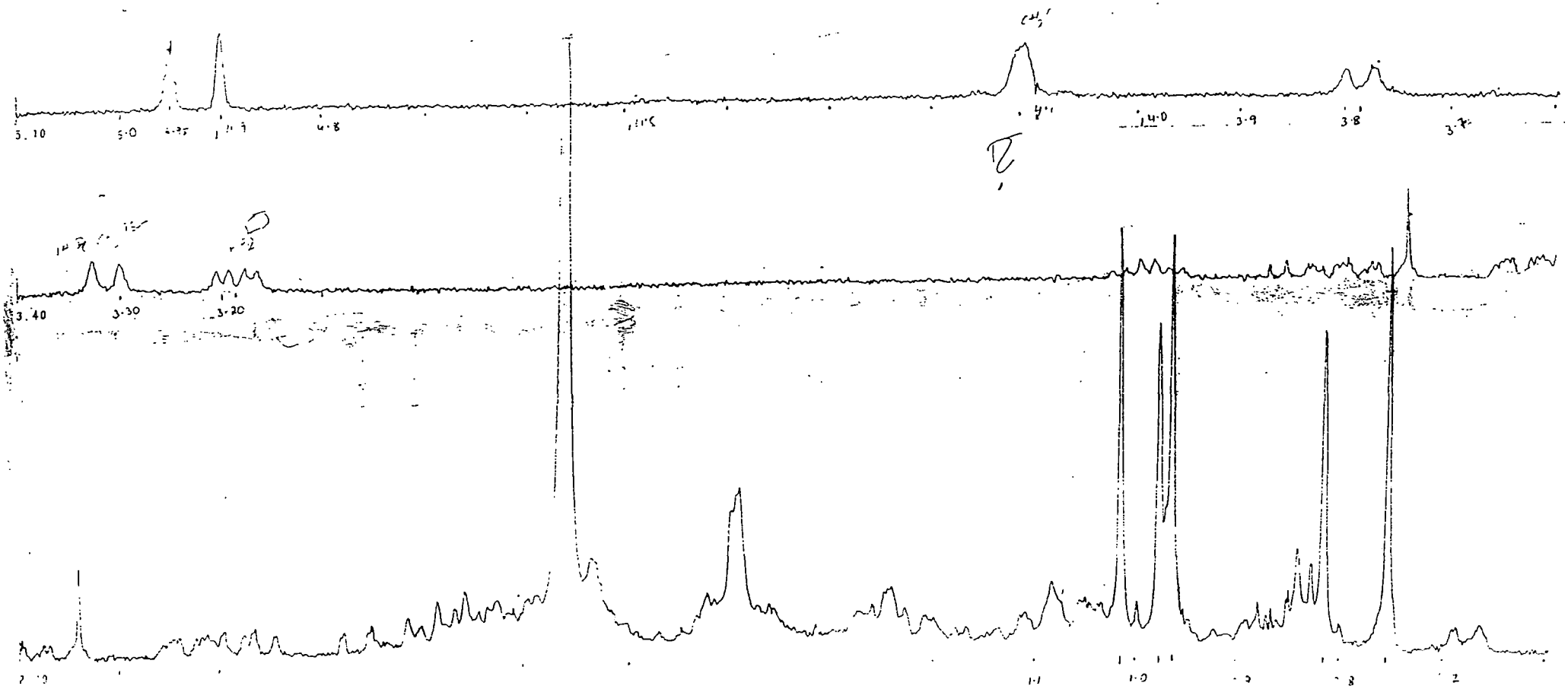


Fig. 18, ^{1}H NMR spectrum of 30-bromo Lup-20(29)-ene 3β,28-diol, 64.

ACTION OF N-BROMOSUCCINIMIDE ON LUPAN-20(29)-EN-3,30-DIYL ACETATE IN DIMETHYL SULFOXIDE.

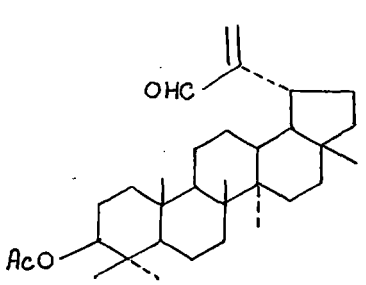
The compound lupan-20(29)-en-3,30-diyl acetate (prepared from lupenyl acetate, see Experimental) **67**, was dissolved in chloroform containing dimethyl sulfoxide and N-bromosuccinimide was added. The mixture was than kept in dark for 24 hours and the product thus obtained was chromatographed, which on elution with benzene afforded a compound-H.

Characterisation of compound H :-

The compound H was repeatedly crystallised from chloroform methanol yielding colourless crystals, *M.P.*224-5^{o} C ; It did not respond to Beilstein test for halogen but produced yellow colouration with TNM. The IR spectrum (fig.**19**) showed peaks at 1730,1700 cm^{-1} for carbonyl group and 1255 cm^{-1} showing that one carbonyl is due to acetate function. Its Mass spectrum (fig.**20**) exhibited molecular ion peak at m/e 482 (M, 24%); Other fragments appeared at 467 (M-CH_3,6%) 422 (M-AcOH,62), 407, 379, 297, 279, 203,189,149,135,121,107,95 (100).

Elemental analysis and Mass spectrum suggested the molecular formula to be $C_{32}H_{50}O_3$. ^{1}H NMR (fig.**21**) signals showed six singlets at (δ in ppm) 0.82, 0.83, 0.84, 0.85, 0.92 and 1.01 for six tertiary methyl groups; one singlet at 2.04 for acetoxy methyl protons; two singlets at 5.93 and 6.31 for two olifinic protons at C-29 is shifted downfield due to the presence of a carbonyl group at the C-30 position. The remaining singlet that appeared douwn field at 9.51 integrated for a single proton was due to the aldehydic proton at C-30.

Thus, from the above spectral studies the compound H, was suggested as lupan-20(29)-en,30-al,3β-yl acetate **65**.

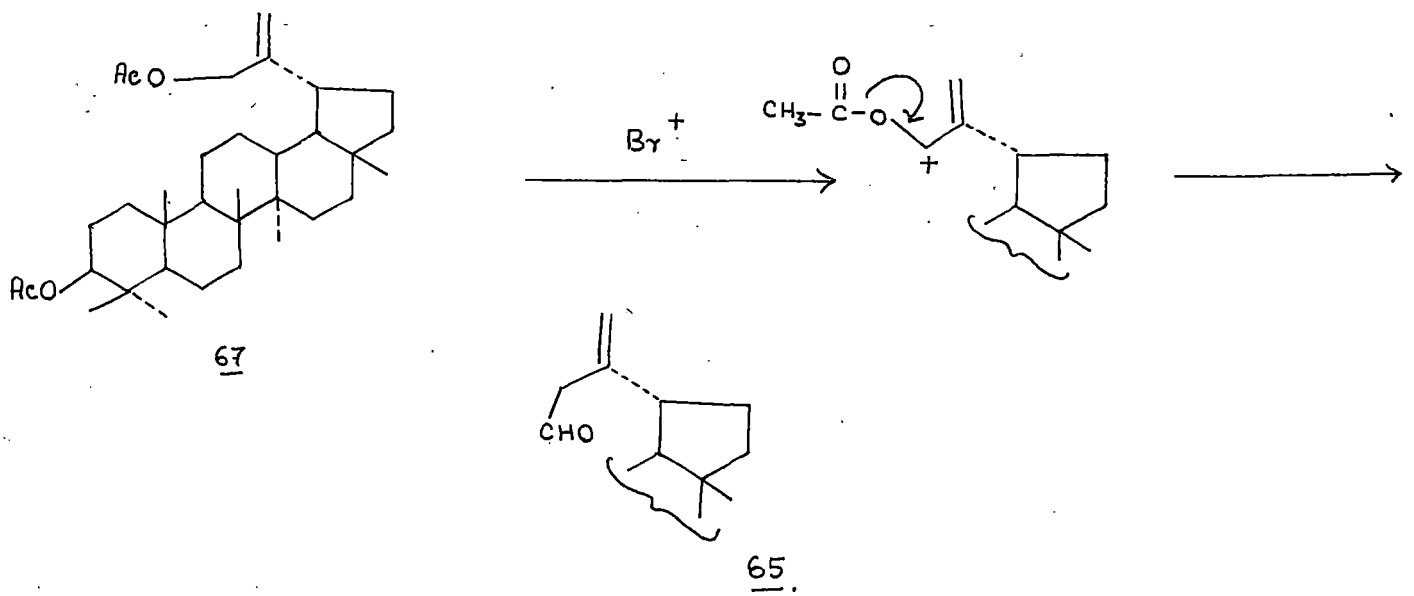


65

Mechanism for the reaction.

It was very interesting to observe that in almost all the reaction with N-bromosuccinimide, a bromonium ion attacks the double bond at 20(29) position or an allylic bromination also takes place but to a lesser extent. However, in the present case only oxidation of C-30 position occurs. In this compound there are two acetate groups of which the one at C-30 was a primary one at allylic position.

When a bromonium ion approaches the π-bond at C-29,30 position the allylic hydrogen atom is preferably removed generating a carbonium ion at C-30 position. This perhaps stabilizes by loss of acetyl group to afford the aldehyde.



67

65.

While, the second possible mechanism may be suggested as follows :-

Since, the dimethyl sulfoxide is not absolutely dried it may contain some water which would cause hydrolysis of 30-hydroxy lupenyl acetate. Thus primary hydroxy group at C-30 position gets oxidised by N-bromosuccinimide to the aldehyde group.

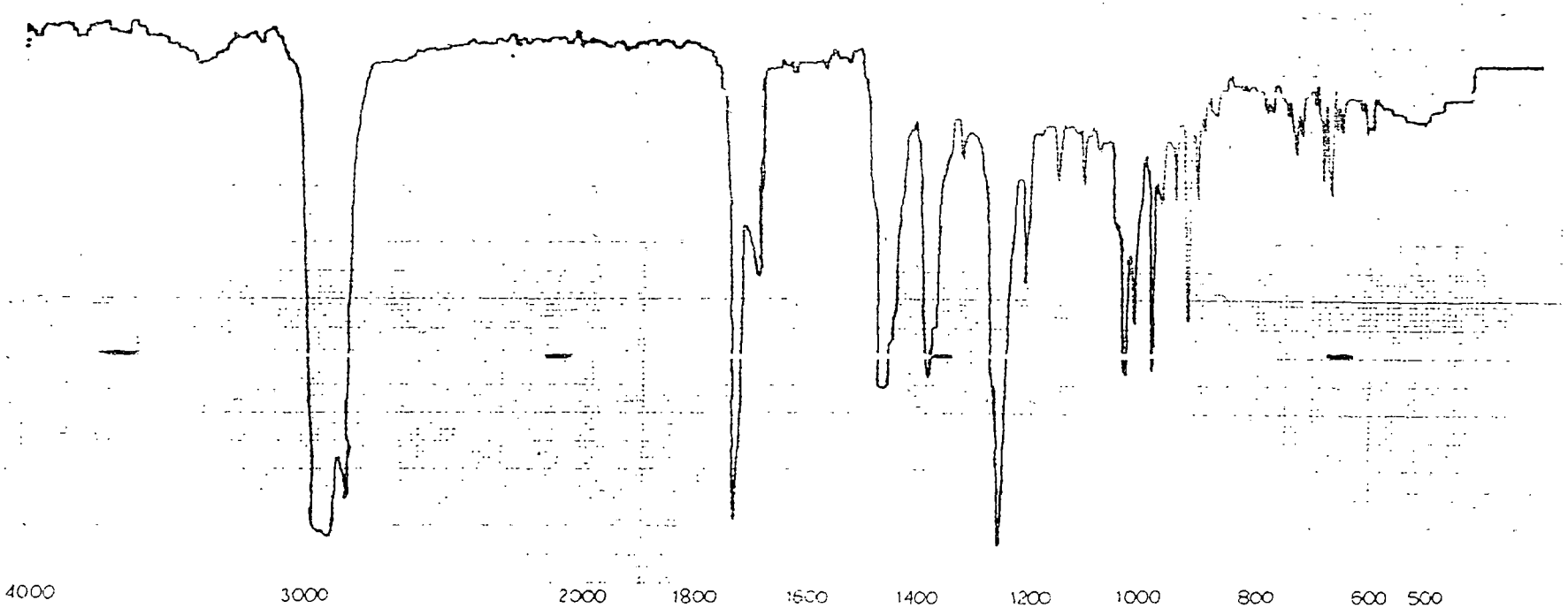


Fig. 19. IR spectrum of lupan 20(29)-en,30-al-3β-yl acetate,65.

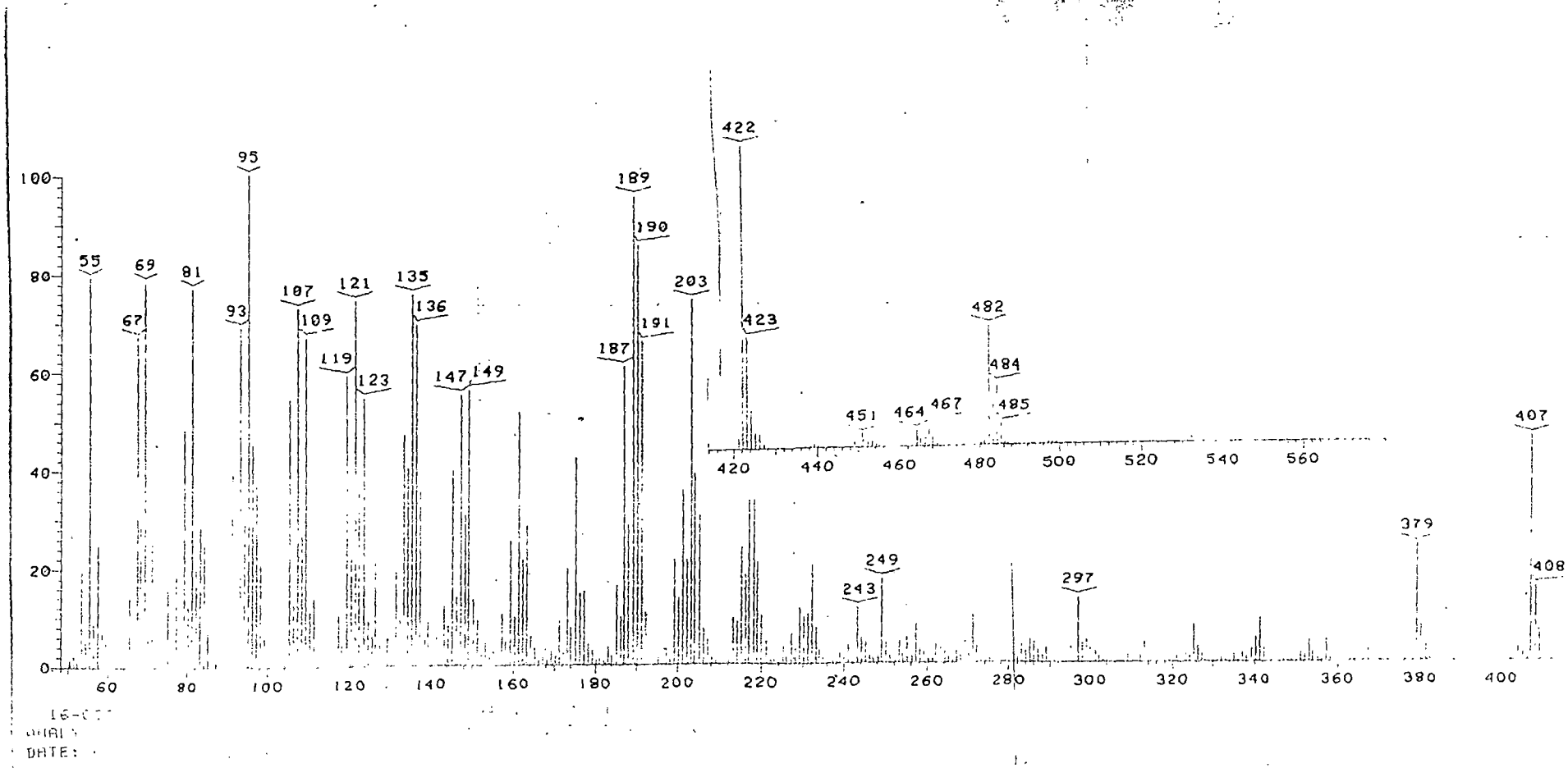


Fig. 20 Mass spectrum of lup 20(29)-en, 30-al, 3β-yl acetate, 65.

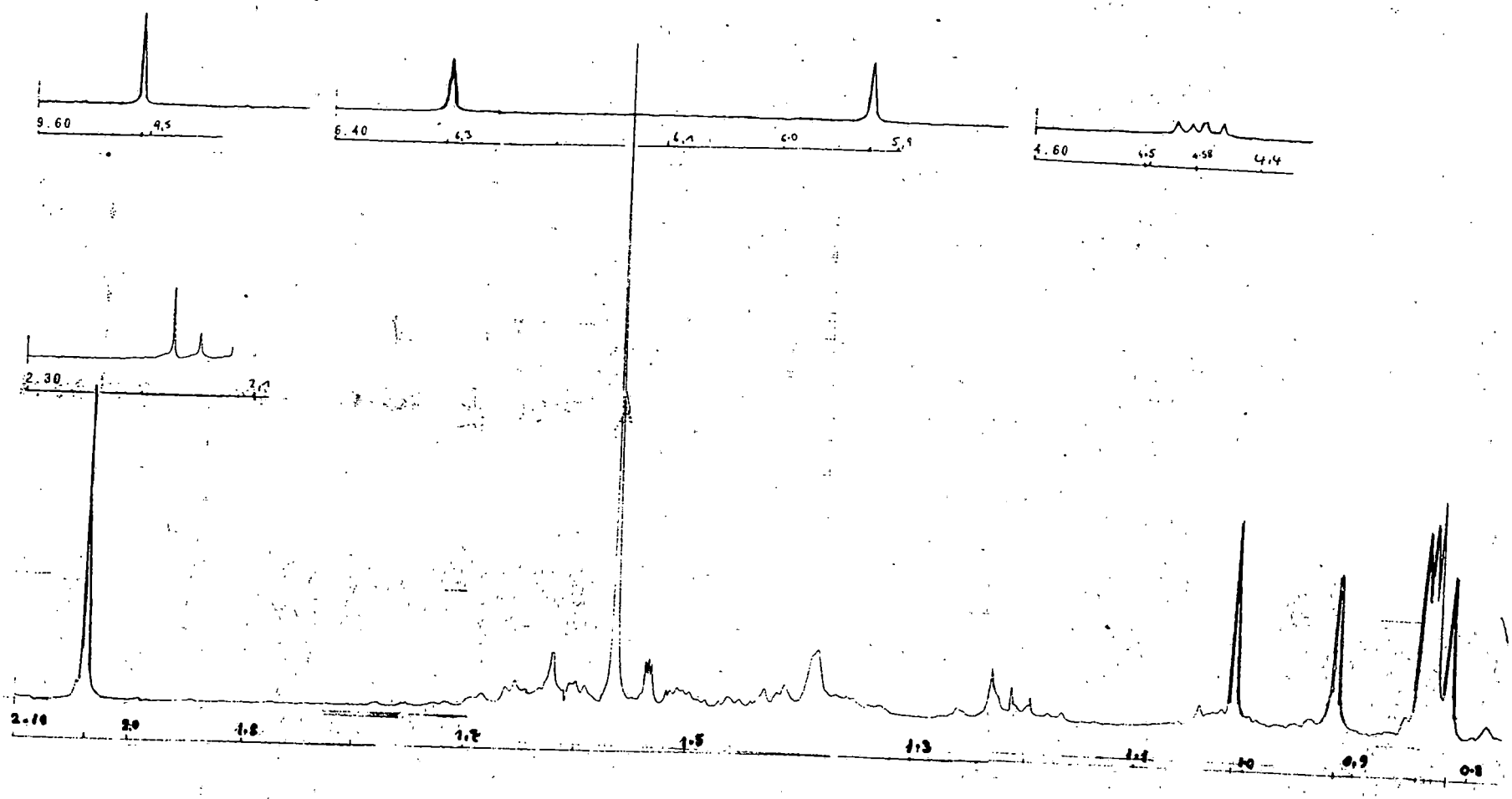


Fig. 21. ^{1}H NMR spectrum of lup-20(29)-en, 30-al, 3β-yl acetate, 65.