STUDIES ON THE OXIDATIVE REACTIONS OF TRITERPENOIDS

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By
Animesh Roy, M.Sc.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF NORTH BENGAL
RAJA RAMMOHUNPUR, DARJEELING
WEST BENGAL, INDIA

Dedicated to

the living memory of my

father Dr. A. B. Roy

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The shortcomings, if any, are entirely the author's.

Department of Chemistry
University of North Bengal
Raja Rammohanpur
Darjeeling.

Animesh Roy,
(ANIMESH ROY)

SUMMARY.

The research work being reported in this thesis has been divided into four parts.

PART-I

OXIDATION OF PENTACYCLIC TRITERPENOIDS HAVING DOUBLE BONDS AT C-2 AND C-3 POSITIONS WITH SELENIUM DIOXIDE IN TERTIARY BUTANOL CONTAINING HYDROGEN PEROXIDE.

Part-I has been divided into three chapters

CHAPTER-I

This chapter comprises a short review of oxidations with selenium dioxide in presence of hydrogen peroxide.

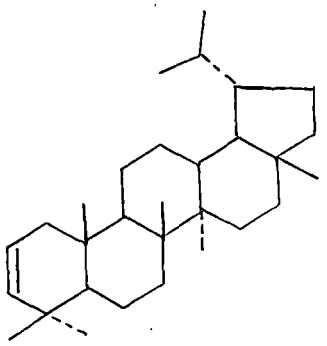
CHAPTER-II

This chapter contains the discussion part on oxidation of Lup-2(3)-ene (1), 2,3 dehydro methyl dihydro betulinate (4), Friedel-3(4)-ene (6), and 3,4 dehydro friedel 27→15-olide (9),in tertiary butanol containing hydrogen peroxide.

SECTION -A :

Lup-2(3)-ene 1, on refluxing with selenium dioxide in tertiary butanol containing hydrogen peroxide afforded a single product characterised as lupan 2β,3α-diol 2, M.P. 245-6°C, which was isolated after acetylation as lupan 2β,3α-diyl acetate 3, M.P. 221-2°C; molecular formula $C_{34}H_{56}O_4$; IR : 1750, 1270 and 1250 cm^{-1} ($-CO-CH_3$); Mass : m/e 528 (M^+, 86%) ;

The structure 3, is established from spectral studies (^1H NMR , Mass and IR). The mode of reaction mechanism and formation of 2 and 3 has also been discussed.



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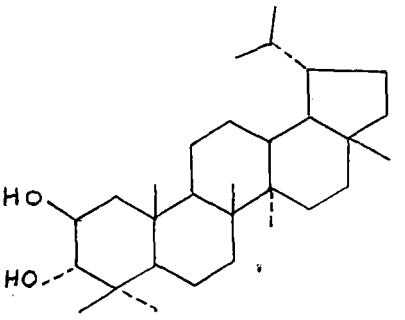

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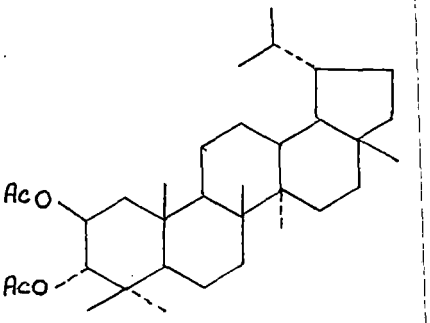

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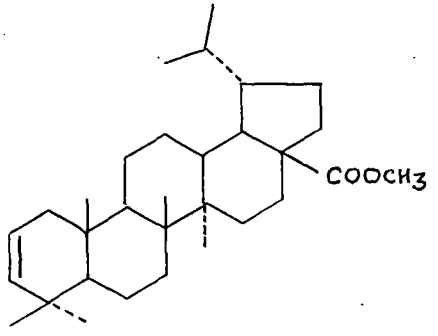
SECTION-B :

In this section the oxidation product of 2,3 dehydro methyl dihydro betulinate (4), is discussed. 4 on oxidation with selenium dioxide in tertiary butanol containing hydrogen peroxide furnished a single product isolated after acetylation as 2β,3α-diacetoxy methyl dihydro betulinate 5, molecular formula $C_{35}H_{56}O_6$, M.P. 209-10°C; IR : 1730, 1710 and 1230 cm^{-1} (-CO-CH_3 and -$COOCH_3$) ; Mass : m/e 572 (M^+, 4%) ; The structure 5 is based on spectral analysis (^1H NMR , IR and Mass)



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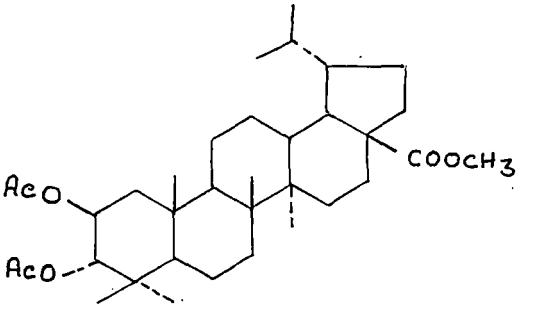

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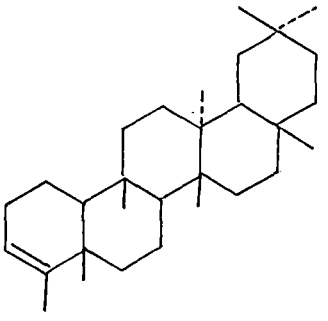
SECTION-C :

Friedel-3(4)-ene (6) on prolong heating with selenium dioxide in tertiary butanol containing hydrogen peroxide furnished two products isolated and characterised as lupanone 7, $C_{30}H_{50}O$, M.P.207-8°C; IR : 1715 cm^{-1}(-CO); Mass :m/e 426 (M^+,14%) and friedelan-3β,4α-diol 8, $C_{30}H_{52}O_2$, M.P. 235-6°C, IR : 3340 and 3380 cm^{-1} (-OH), Mass : m/e 444 (M^+,72%), from ^1H NMR, Mass and IR spectral studies.



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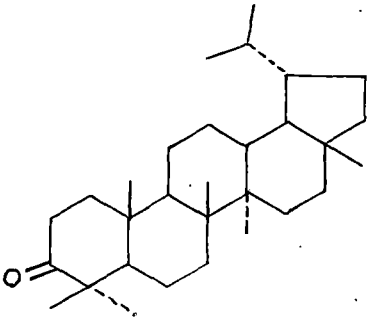

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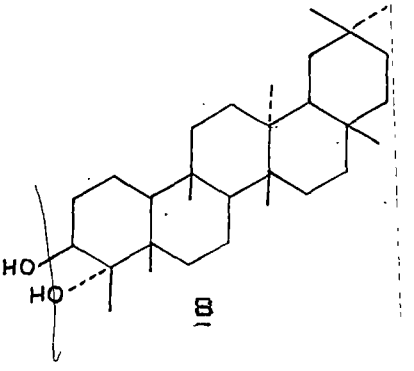

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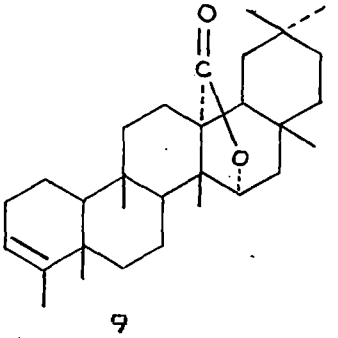
Their formation and probable mechanism are also suggested in this section.

SECTION-D :

3(4)-dehydro friedelan 27→15-olide (9),on similar treatment under identical condition afforded a single product isolated and characterised as friedelan 3β,4α-dihydroxy 27→15-olide **10**, $C_{30}H_{48}O_4$, M.P. 270-1°C; IR : 3500, 3440 (-OH) and 1760 cm^{-1} (γ-lactone), Mass : 472 (M^+, 22%).



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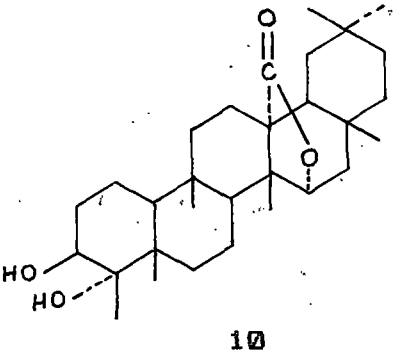

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The structure **10** is based on Mass, IR, ^1H NMR, and ^{13}C NMR spectral analysis.

CHAPTER-III

This chapter describes the experimental details of the work discussed in CHAPTER-II

PART-II

ACTION OF N-BROMOSUCCINIMIDE ON PENTACYCLIC TRITERPENOIDS OF LUPANE AND FRIEDELANE SKELETON IN DIMETHYL SULFOXIDE.

Part-II has been divided into three chapters.

CHAPTER-I.

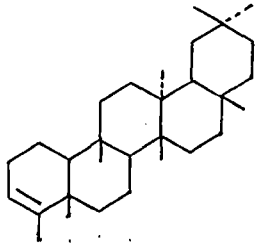
This chapter constitutes a brief review of previous related works done with N-bromosuccinimide.

CHAPTER-II

Studies on the action of N-bromosuccinimide on friedel-3(4)-ene (**11**), 30-bromolupenyl acetate (**14**), lupan 20(29)-ene,3β,28-diol (**16**), lupan 20(29)-ene,3β,28-diyl acetate(**18**) and lupan 20(29)-ene,3β,30-diyl acetate (**21**) taken in dimethyl sulfoxide.

SECTION-A :

Friedel-3(4)-ene (**11**) was taken in dimethyl sulfoxide and kept in dark for 24 hours with N-bromosuccinimide. After the reaction two products were isolated and characterised as 3α-bromo olean-13(18)-ene **12**, molecular formula $C_{30}H_{49}Br$, M.P. 200-1^{o}C; responded to Beilstein test for halogen and gave yellow colouration with tetranitromethane (TNM), Mass : m/e 490 (M_1^+, Br^{79},) and 488 (M_2^+, Br^{77}) and 3β-hydroxy olean-12(13)-ene **13**, $C_{30}H_{50}O$, M.P. 229-30^{o}C, TNM test positive but Beilstein test for halogen negetive, IR : 3380 cm^{-1} (-OH), Mass : m/e 411 (M^+, 11%).



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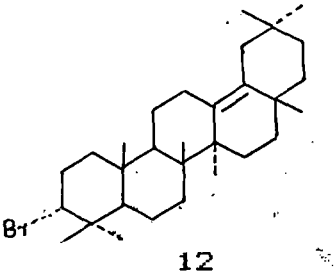

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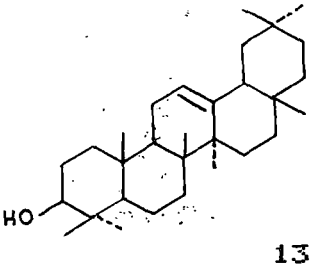

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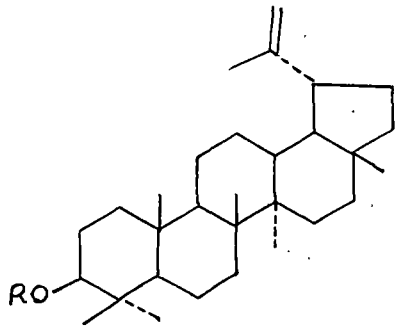
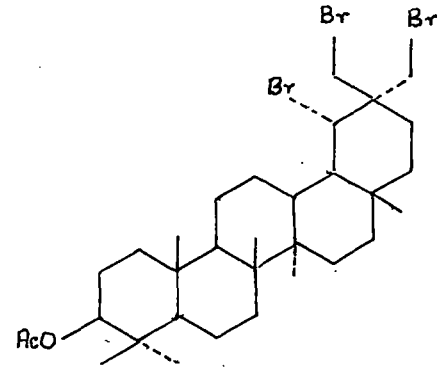
SECTION-B :

Lupenyl acetate (**14a**),(prepared from lupeol,**14** see Experimental) was dissolved in acetic acid cooled at $0^{o}(-5)^{o}C$ and bromine was added. After the reaction a single product was isolated which was identified as 3β-acetyl 19α,29,30 tribromo oleanane **15**, molecular formula $C_{32}H_{51}O_2Br_3$,M.P. 225-6°C, IR :1690 and 1255 cm^{-1} ($-COCH_3$), Beilstein test for halogen was positive but did not respond to TNM test, Mass : m/e 710 (M_1^+,Br^{79}) and 708 (M_2^+,Br^{77}).



14, R = H

14a, R = Ac



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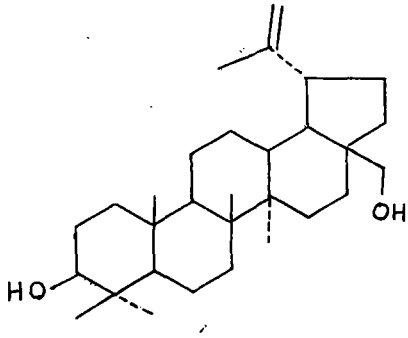
SECTION-C :

Lupan 20(29)-en,3β,28-diol (**16**),on similar treatment under identical condition furnished a product isolated and identified as 3-keto oleanan 28-19-oxo,29,30 dibromide **17**, $C_{30}H_{46}O_2Br_2$, M.P. 232-3°C IR : 1720 cm^{-1} (-C=O) ; Beilstein test for halogen was positive but TNM test negetive ; Mass : m/e 599 (M_1^+,Br^{79}, 2%) and 597 (M_2^+,Br^{77},6%);



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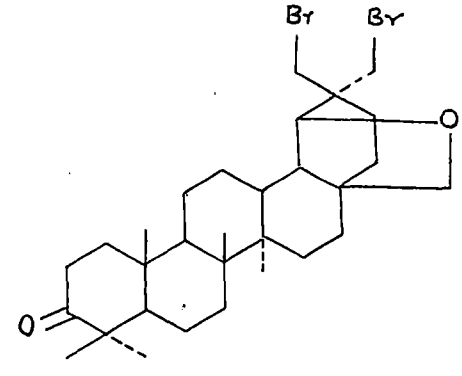

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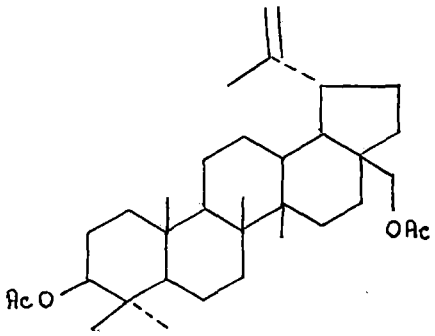
SECTION-D :

Lupan 20(29)-en,3β,28-diyl acetate (**18**), on similar treatment under identical condition afforded two compounds **19** and **20**.
They were identified as 30-bromo lupan 20(29)-en-3β,28-diyl acetate **19**, $C_{34}H_{53}O_4Br$, M.P. 169-70°C ; IR : 1730 and 1240 cm^{-1} ($-COCH_3$), Mass : m/e 606 (M_1^+, Br^{79}, 0.8%) and 604 (M_2^+, Br^{77}, 1.6%) and 30-bromo lupan 20(29)-en- 3β,28-diol **20**, $C_{30}H_{50}O_2Br$, M.P. 202-3°C ; Beilstein test was positive and produced yellow colouration with TNM, IR : 3390 cm^{-1} (b, -OH); Mass : m/e 442(M_1^+) or 440 (M_2^+) which was less than actual molecular ion mass probably due to loss of one HBr^{79} or HBr^{77} unit.



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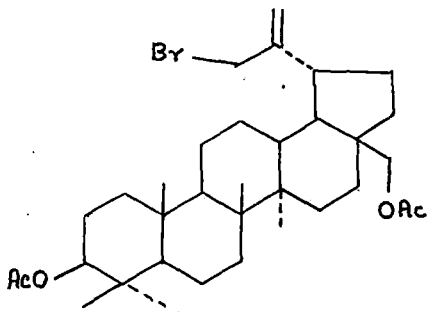

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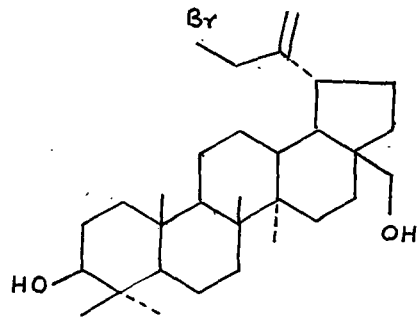

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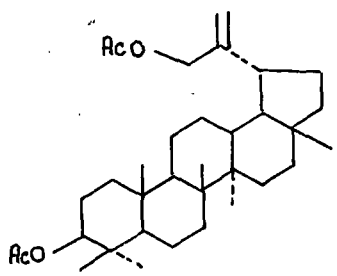
SECTION-E :

lupan 20(29)-en,3β,30-diyl acetate (**21**), on similar treatment with N-bromosuccinimide in dimethyl sulfoxide furnished a compound identified as lupan 20(29)-en,30-al,3β-yl acetate **22**, $C_{32}H_{50}O_3$, M.P. 224-5°C, Beilstein test for halogen was negetive but produced yellow colouration with TNM indicating presence of double bond. IR :1730 cm^{-1} (-CHO) and 1700, 1255 cm^{-1} ($-COCH_3$), Mass : m/e 482 (M^+, 24%).



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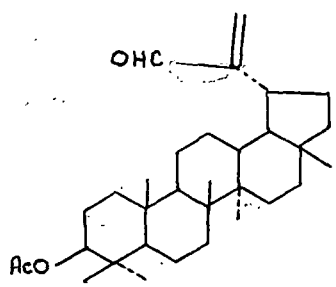

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All the above structures are establlished from Mass, IR, ^{1}H NMR and ^{13}C NMR spectral analysis.

CHAPTER-III

This chapter constitutes the experimental details of research work described in CHAPTER-II.

PART-III

OXIDATION OF PENTACYCLIC TRITERPENOID KETONE, LACTONE AND ESTER WITH META CHLOROPERBENZOIC ACID IN CHLOROFORM.

Part-III has been divided into three chapters.

CHAPTER-I

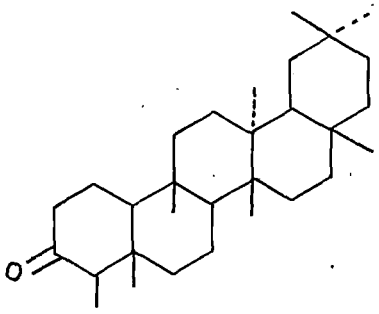
It contains a brief review of oxidation of triterpenoids with meta-chloroperbenzoic acid in different solvents.

CHAPTER-II

This chapter contains the discussion on oxidation of friedelin (23), 3-oxo friedelan 27→15-olide (25) and acetyl methyl betulinate (27) with meta-chloroperbenzoic acid.

SECTION-A :

Friedelin (23), was refluxed with meta-chloroperbenzoic acid in chloroform for 6 hours and after the reaction the single product obtained was identified as 3,4 seco friedelan 3→4-olide 24, $C_{30}H_{50}O_2$, M.P. 271-2°C, IR : 1720 cm^{-1} (ε-lactone) ; Mass : m/e 442 (M^+, 30%). by comparing with authentic sample (M.M.P. and Co-IR)



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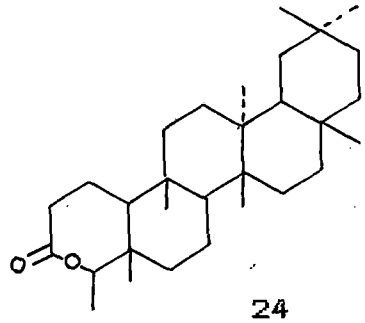

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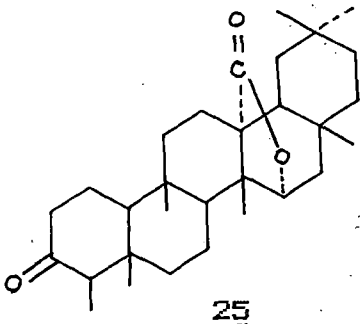
SECTION-B :

3-oxo friedelan 3 → 4-olide (25), (odolactone) on similar treatment afforded a single product, which was identified as friedelan 3→4,27→15-diolide 26, $C_{30}H_{46}O_4$, M.P.>300°C, IR : 1760 and 1730 cm^{-1} (ε and γ-lactone); Mass : 470 (M^+).



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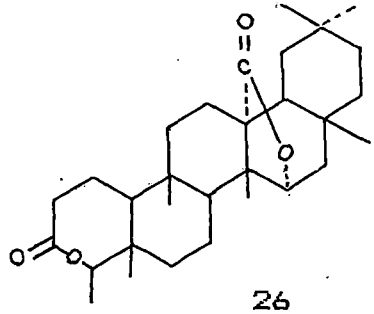

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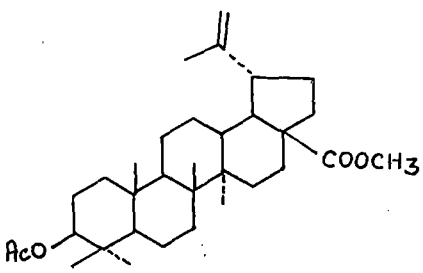
SECTION-C :

Acetyl methyl betulinate (27) on similar treatment under identical condition furnished two products characterised as 29-nor-3β-O-acetyl-lupan-20-O-formyl 28 methyl carboxylate 28, $C_{33}H_{54}O_6$, M.P. 151-2°C, did not respond to TNM test, IR : 1740, 1250 cm^{-1} ($-COCH_3$); Mass : m/e 544 (M^+) and 29-nor acetyl methyl 20-oxo-betulinate 29, $C_{32}H_{50}O_5$, M.P. 211-2°C; IR : 1730, 1260 cm^{-1} ($-COCH_3$), did not produce yellow colouration with TNM. Mass : m/e 514 (M^+).



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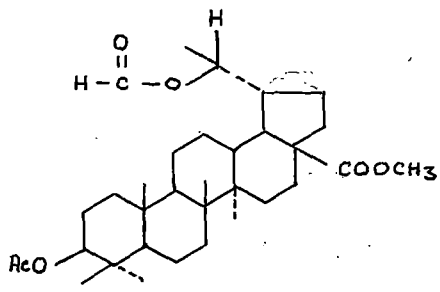

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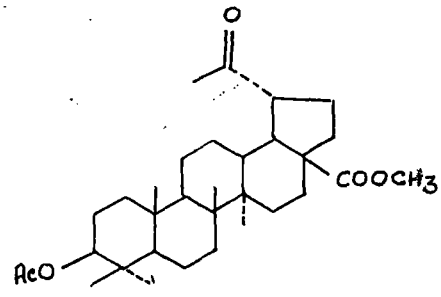

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All the 24, 26, 28 and 29 structures are based on ^{1}H NMR, Mass and IR spectral studies.

CHAPTER-III

Experimental details of work described in CHAPTER-II.

PART-IV

REDUCTIVE CLEAVAGE OF SEVEN MEMBERED LACTONE RING WITH LITHIUM IN ETHYLENEDIAMINE.

This part is also divided in three chapters

CHAPTER-I

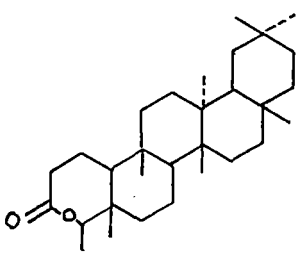
It constitutes a short review of lithium ethylenediamine as a reducing agent.

CHAPTER-II

This chapter contains studies on reductive cleavage of 3,4 seco friedelan 3→4-olide (30) and friedelan 3→4, 27→15-diolide (32) with lithium in ethylenediamine.

SECTION A :

3,4 seco friedelan 3→4-olide (30) was refluxed with lithium metal dissolved in dry ethylenediamine for 2 hours over heating mentle. After reaction the product obtained was identified as 3,4 seco friedelan 3,4 diol 31, $C_{30}H_{50}O_2$, M.P. 173-4°C, IR : 3420 cm^{-1} (broad) (-OH); Mass : m/e 428 $(M-H_2O)^+$.



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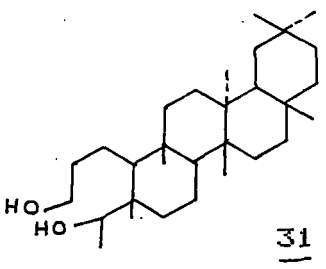

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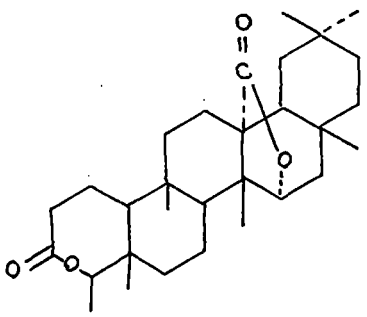
SECTION-B :

Friedelan 3→4,27→15 diolide (32) was reduced with lithium metal dissolved in dry ethylenediamine at room temperature and the product obtained was isolated after acetylation. It was identified as friedelan 3,4 diacetoxy 27→15-olide 33, $C_{34}H_{54}O_6$, M.P.241-2°C , IR : 1750 cm^{-1} ($-COCH_3$); Mass : m/e 558 (M^+, 7%).



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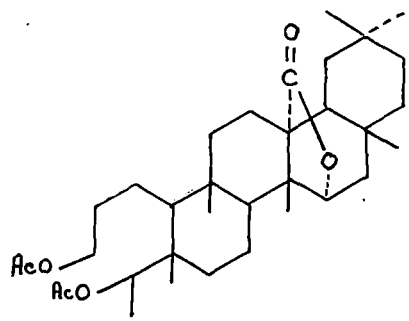

33

Both the structures 31 and 33 are established from ^1H NMR, Mass and IR spectral analysis.

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The experimental details of the above two lactone cleavage are described in this chapter.

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PART-I

OXIDATION OF PENTACYCLIC TRITERPENOIDS HAVING DOUBLE BONDS AT C-2 AND C-3 POSITIONS WITH SELENIUM DIOXIDE IN TERTIARY BUTANOL CONTAINING HYDROGEN PEROXIDE.

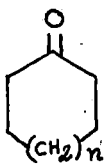
CHAPTER-I

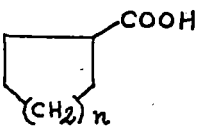
A SHORT REVIEW ON REACTIONS OF SELENIUM-DIOXIDE IN PRESENCE OF HYDROGEN-PEROXIDE.

The selenium dioxide(SeO_2) catalysed reaction of hydrogen peroxide (H_2O_2)has been widely used for performing various oxidative transformations. A brief description of some oxidative transformations are summerised below.

Seguin[1] prepared trans cyclohexanediol free of cis-compound from cyclohexene using H_2O_2 in presence of SeO_2 and also prepared 1,2 diols cyclopentadiene from cyclopentadiene.

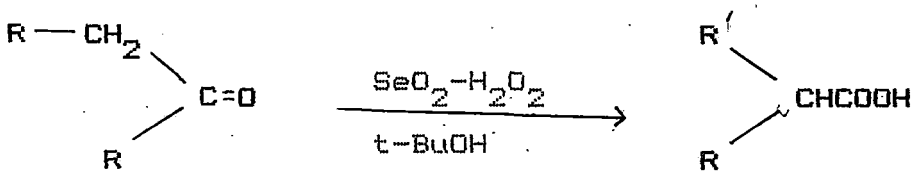
Curtis et al[2] used SeO_2, as catalyst in presence of hydrogen peroxide to oxidise acrolein and methacrolein to monomeric acrylic and methacrylic acids and suggested that at first selenious acid oxidised to selenenic acid with H_2O_2 than that selenenic acid reacted with acrolein to give acrylic acid and selenious acid. Payne et al[3] investigated the oxidation of cycloheptanone,cyclohexanone and cyclo pentanone with SeO_2 in presence of H_2O_2 and anticipated that the cyclic ketones might undergo the well known reaction with SeO_2 giving α-diketones with H_2O_2 serving merely to oxidise selenium metal back to dioxide. They[3] observed that along with other competing reactions,all three ketones underwent oxidative ring contraction to cyclohexane, cyclopentane and cyclobutane carboxylic acids in 34,32 and 23% yields, respectively.





n = 2, 34%
n = 1, 32%
n = o, 23%

Sonoda et al[4] studied oxidation of aliphatic ketones, RCH_2COR' with H_2O_2 in presence of SeO_2 in tertiary butanol solvent(t-BuOH) and got carboxylic acids,RRCHCOOH accompanied by rearrangment of alkyl groups.



Where R = H, R′ = R = alkyl group

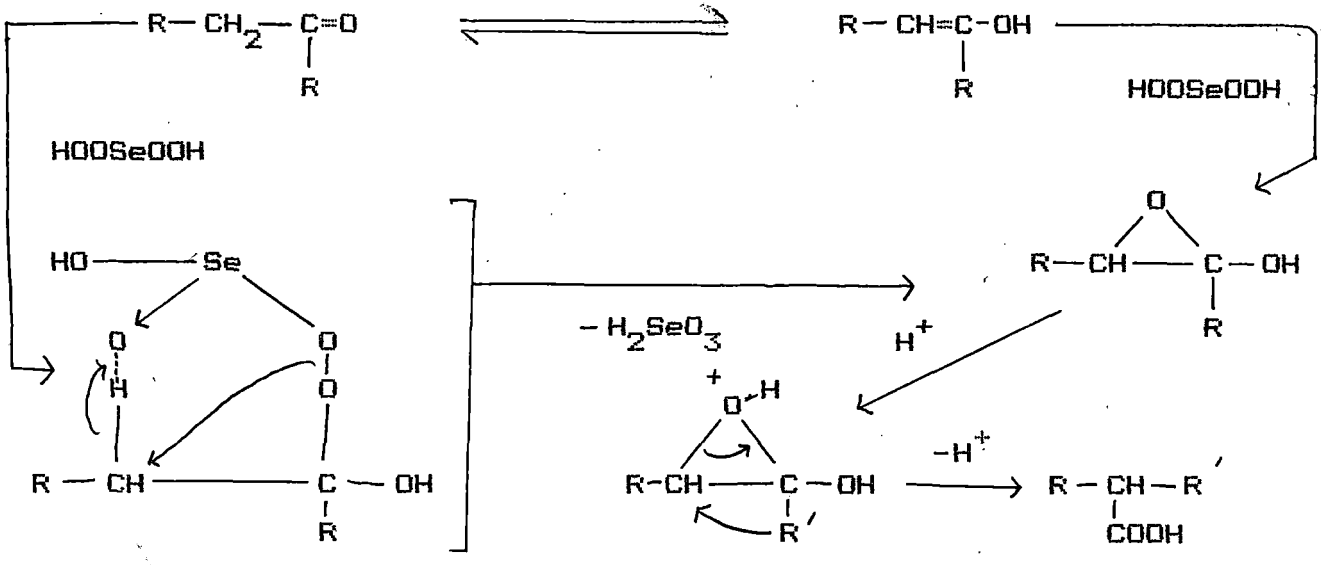
They[4] used acetone, methyl ethyl ketone, methyl-n-propyl ketone, and diethyl ketone as starting material. They suggested that the main rearrangement observed was due to migration of the alkyl group having smaller number of carbon atoms to the α-carbon atom of the larger number of carbon atoms; to the small one also occurred in some degree. These workers shared the view of Hughes and Martin[5] who proposed the formation of peroxy selenious acid **1** from SeO_2 by the action of H_2O_2.

$$SeO_2 + H_2O_2 \rightleftharpoons HOOSeOOH$$

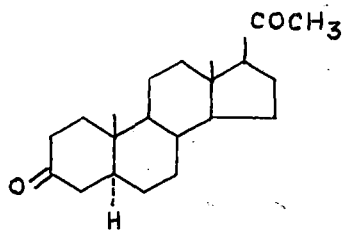
1

The following mechanism was presumed by these workers as shown in scheme -I

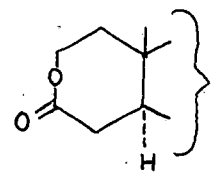
SCHEME-I



Caspi et al[6,7] reported that steroidal 3-Ketones in the 5α and 5β-series with H_2O_2 in presence of SeO_2 gave ring-A contracted acids and products of bond scission on either side of the carbonyl group. The compound with A/B - trans junctions, 17β- acetoxy 5α- androstan -3-one **2a** gave lactone **3** and two carboxylic acids **4** and **5**. The oxidation of 17β-acetoxy -5β- androstan -3- one **2b**, gave lactone **6** as single product.



2a = 5α, 2b = 5β,



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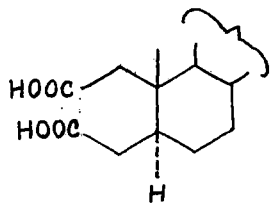
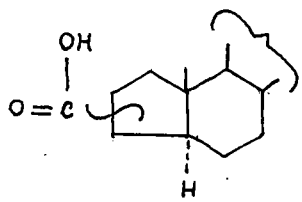
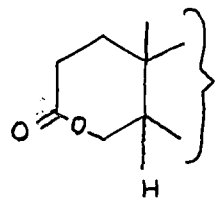


4,

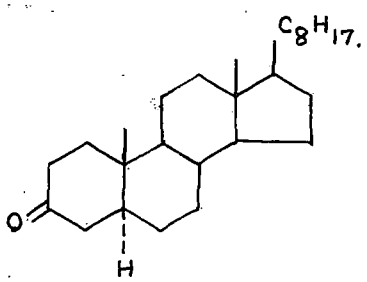


5,

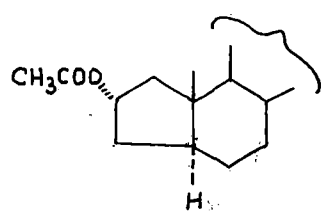


6,

Jerussi et al[8] studied the oxidation reaction of 5α-cholestan-3-one 7 with selenenic acid and 30% H_2O_2 in tertiary butanol. They found a complex mixture of acids which on esterification gave 2α- carbomethoxy -A-nor- 5α- cholestane, 8 in 35% yield, 3β- carbomethoxy-A-nor-5α- cholestane 9 in 4% yield and methyl 2,3-seco-5α-cholestane 2,3 - dioate 10a in 8% yield.



7,



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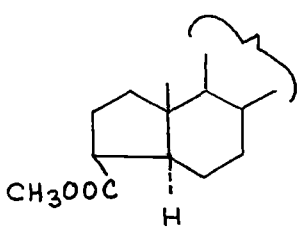
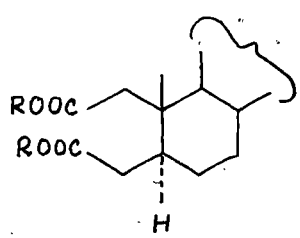


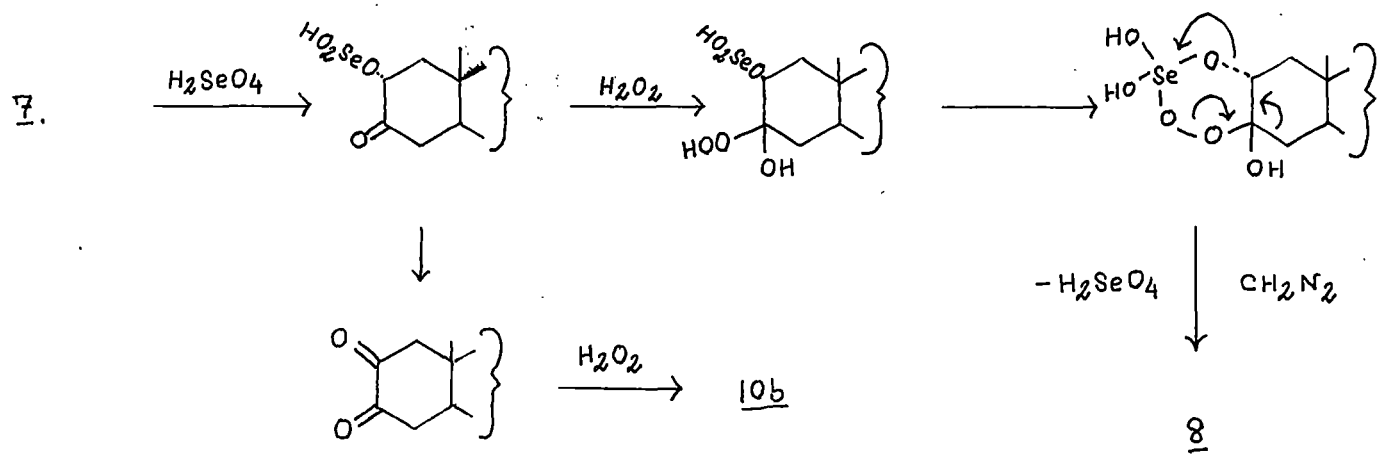
9,



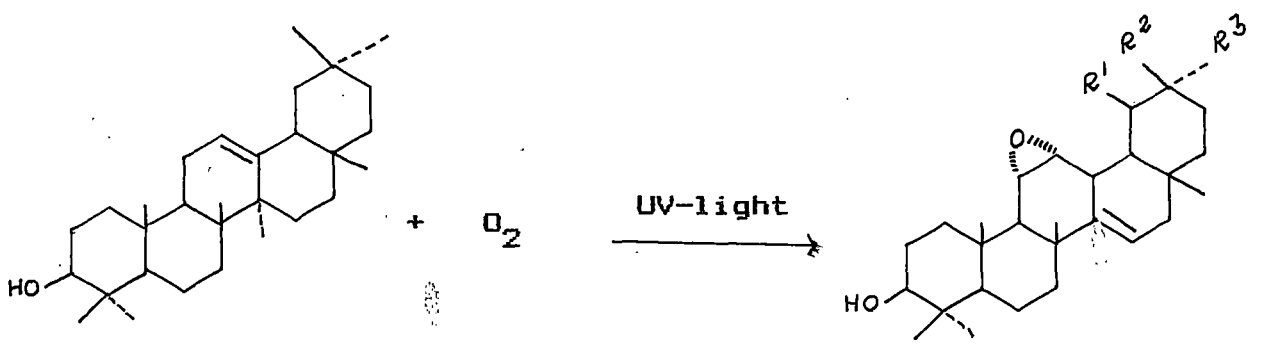
10a, R=CH_3, 10b, R=H.

The mechanism proposed by Jerussi et al[8] are summerised in the Scheme -II

SCHEME-II



Corey et al[9] reported the formation of a new photoxidation product 12, obtained by irradiation of acidified ethanolic solution of β-amyrin 11 for 2-3 weeks with Ultra - Violet Lamp (through pyrex glass)



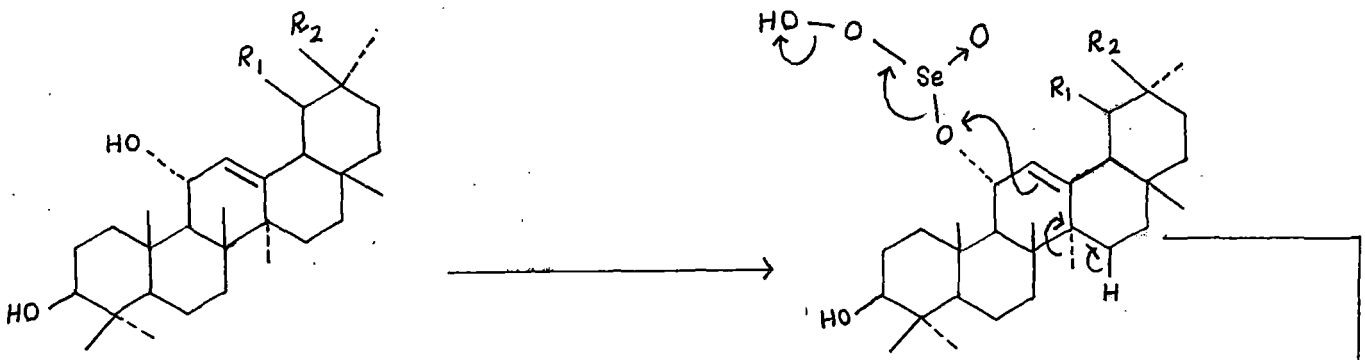
11, 12, R_1= CH_3, R_2=H, R_3= CH_3.

13, R_1= H, R_2= CH_3, R_3 = CH_3.

They[9] also reported the formation of 13 in small amount by photoxidation of α-amyrin and establised the structure as 13 by chemical and spectral analysis.

They[9] further synthesised the compounds 12/13 from olean

12-en-3β,11α-diol **14a** / Urs-12-en-3β,11α-diol **14b** by treatment with a mixture of hydrogen peroxide and selenious acid in t-BuOH. The mechanism first proposed was as follows:-

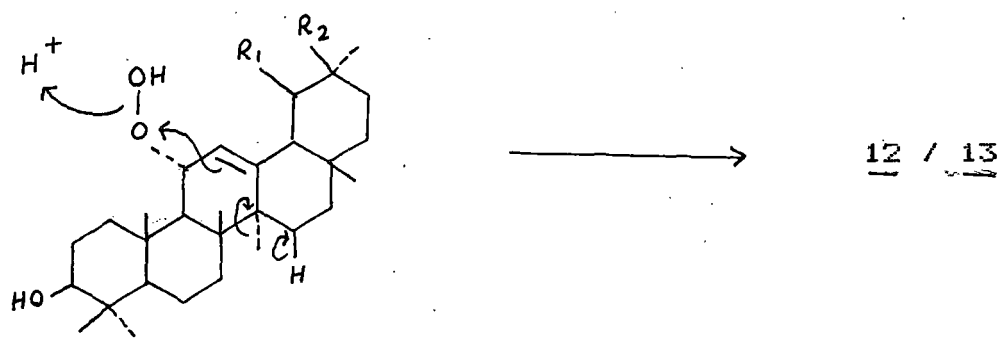


14a, R_1 = H, R_2 = CH_3

14b, R_1 = CH_3, R_2 = H

12 / **13**,

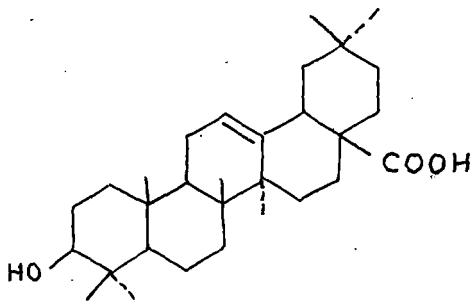
However, this was shown not to be the actual mechanism of the formation **12**/**13** from 3β,11α-diol **14a**/**14b** from the fact that the reaction of the 11-epimeric 12-en-3β,11β-diol with the same reagent also afforded the same product **12**/**13** and not the epimeric epoxide. It evidently shows that the C_{11}-O bond is broken during the reaction. This suggested an alternative mechanism in which the isomeric diols furnish the same C-11,12,13 allylic cation which reacts with the peroxide to form 12-en-3β-ol-11α - hydroperoxide **15**. This in turn undergoes acid catalysed O-O bond fission and carbon rearrangment to give **12**/**13**



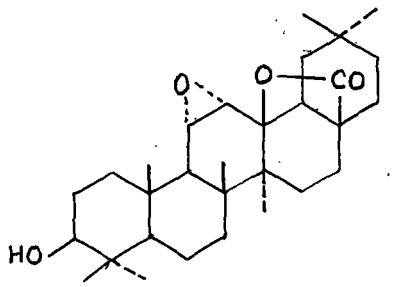
15,

They suggested[9] that selenious acid merely functioned as an acid catalyst and could be replaced by other acids.

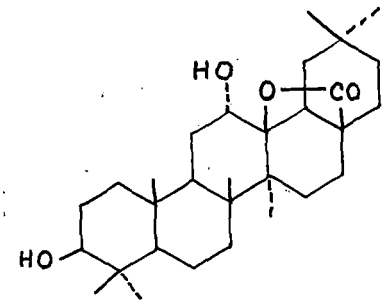
Kitagawa et al[10] studied the photoxidation of oleanolic acid 16 and reported two products 17,18 together with starting material.



16,

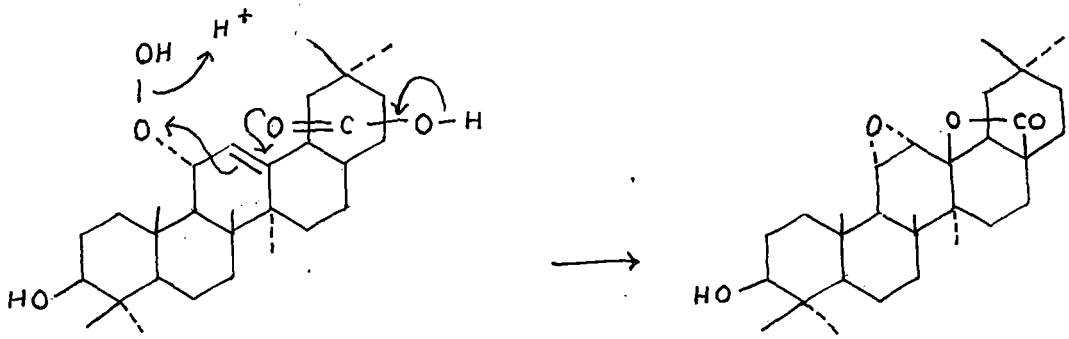


17,



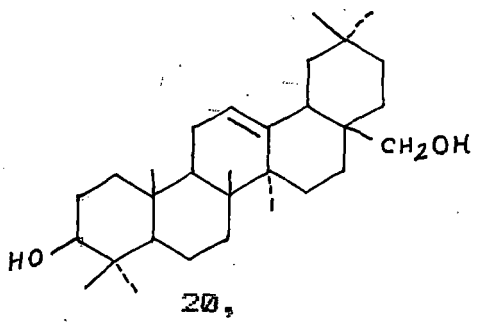
18,

They[10] suggested that the formation of 17 from 16 took place via hypothetical intermediate 19 in which carboxylic function at C-17 was participating .

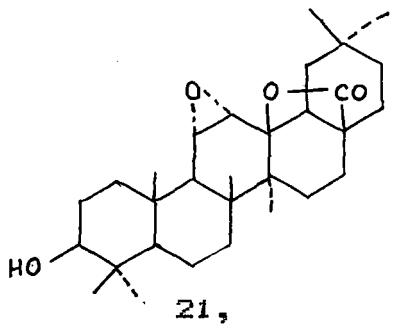


19, 18,

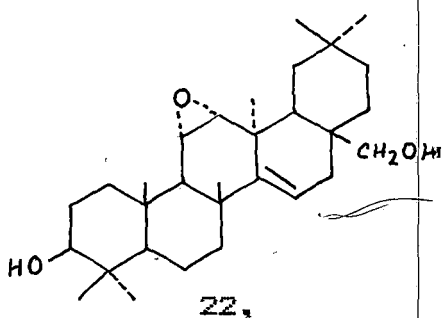
Irradiation of erythrodiol 20 for 100 hours afforded two products 21 and 22 together with starting material.



20,

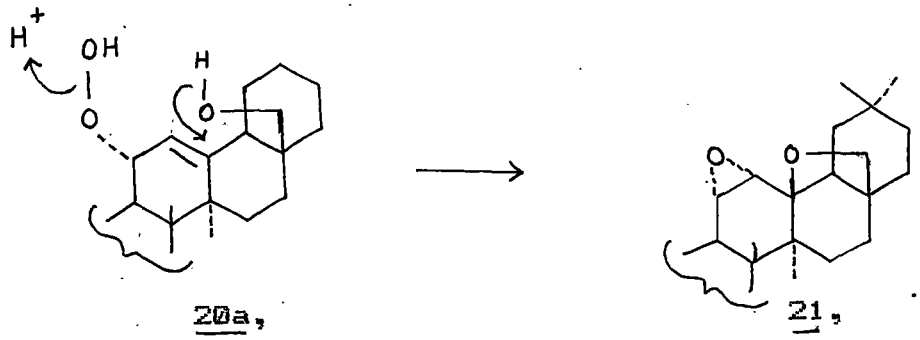


21,



22,

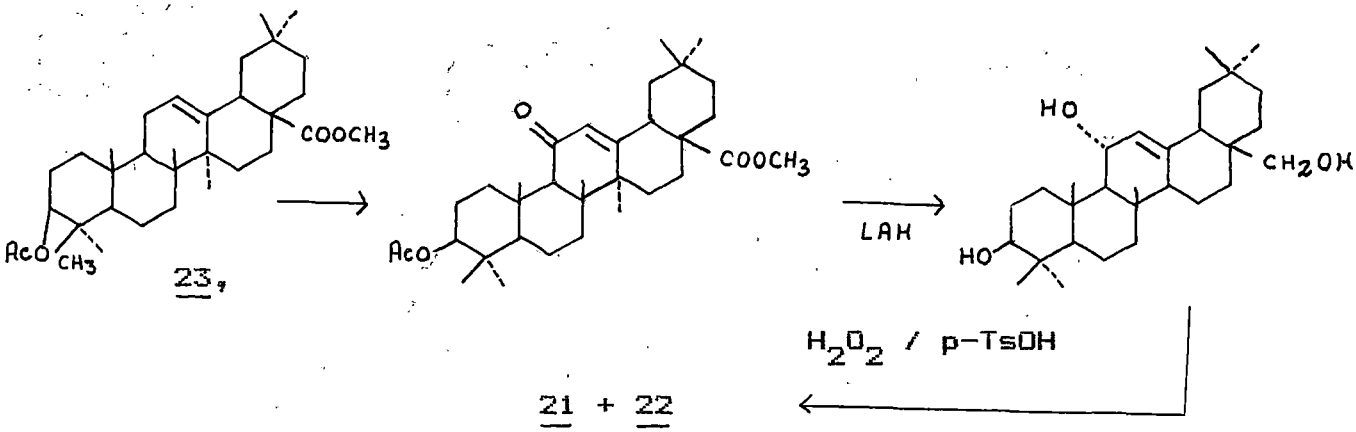
They[11] suggested that the formation of 21 from 20 took place via intermediate 20a in which unshared electron pair of 17β-CH_2OH was participating



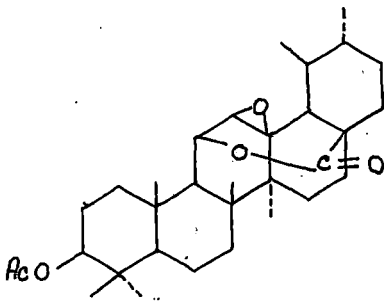
20a, 21,

Kitagawa et al [12] synthesised 21 and 22 from methyl-3-O-acetyl oleanolate 23. as shown in the scheme-III

SCHEME-III



Jeger et al[13] studied the action of H_2O_2 on ursolic acid acetate 24a in hot glacial acetic acid and reported the isolation of three compounds designated as U_1 ($C_{32}H_{48}O_5$), U_2 ($C_{32}H_{50}O_5$), U_3 ($C_{32}H_{50}O_5$) and assigned the structures 25 and 26 for U_1 and U_3 respectively and did not assign any structure for U_2. But Simonsen et al[14] disapproved *structure* 25 for U_1 and suggested the structure 27 or 28 for U_1 without providing any positive evidence in support of their proposition. So Majumder et al[15] reinvestigated this work and isolated U_1, U_2 and methylester of U_3. They revised the structure of U_1 and established the structures of U_2 and U_3 from spectral and chemical analysis.



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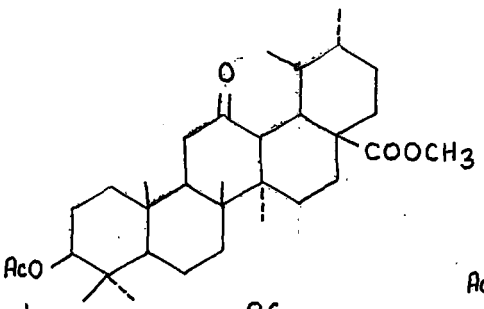

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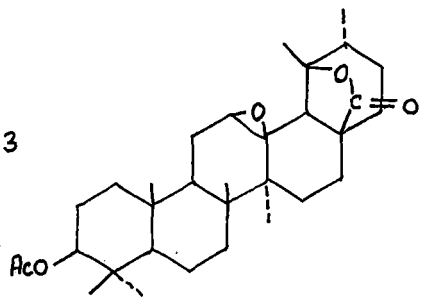
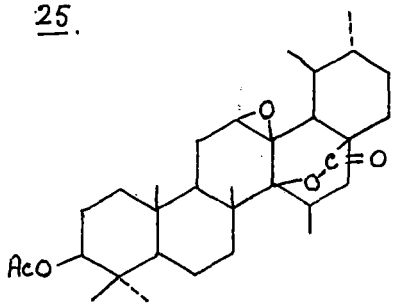
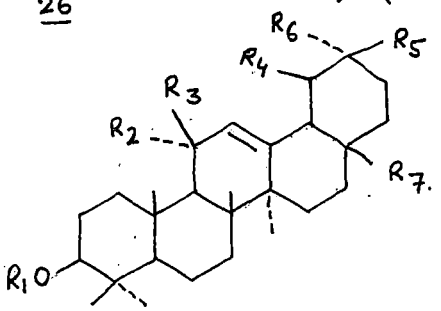


27.



28.



24a, R_1 = Ac, R_2 = R_3 = R_5 = H
R_4 = R_5 = Me, R_7 = COOH

24b, R_1 = Ac, R_2 = R_3 = R_4 = H
R_5 = R_6 = Me; R_7 = COOH

24c, R_1 = R_2 = R_3 = R_5 = H
R_4 = R_6 = Me, R_7 = CH_2OH

24d, R_1 = R_2 = R_3 = R_5 = H
R_4 = R_6 = Me, R_7 = CH_2OAc

24e, R_1 = Ac, R_2 = R_3 = R_5 = H.
R_4 = R_6 = Me, R_7 = CH_2OH.

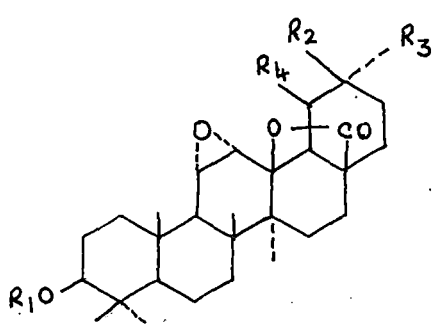
24f, R_1 = Ac, R_2 = R_3 = R_5 = H.
R_4 = R_6 = Me, R_7 = CH_2OAc.

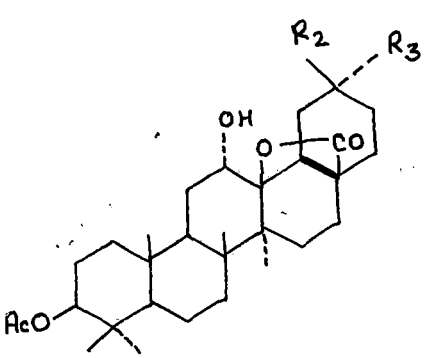
24g, R_1 = Ac. R_2 = R_3 = R_4 = H.
R_5 = R_6 = Me, R_7 = CH_2OH

24h, R_1 = R_2 = R_3 = R_4 = H.
R_5 = R_6 = Me, R_7 = CH_2OAc

24i, R_1 = Ac, R_2 = R_3 = R_4 = H, R_5 = R_6 = Me, R_7 = CH_2OAc.

Majumder et al[15] suggested structure 3β-acetoxy 11α-12α epoxy ursan--28-oic-13(28)-lactone **29a** for U_1 ;
3β-acetoxy-12α-hydroxy-ursane-28-oic-13 (28)-lactone **30a** for U_2 and **26** for U_3 from PMR and other physical data.



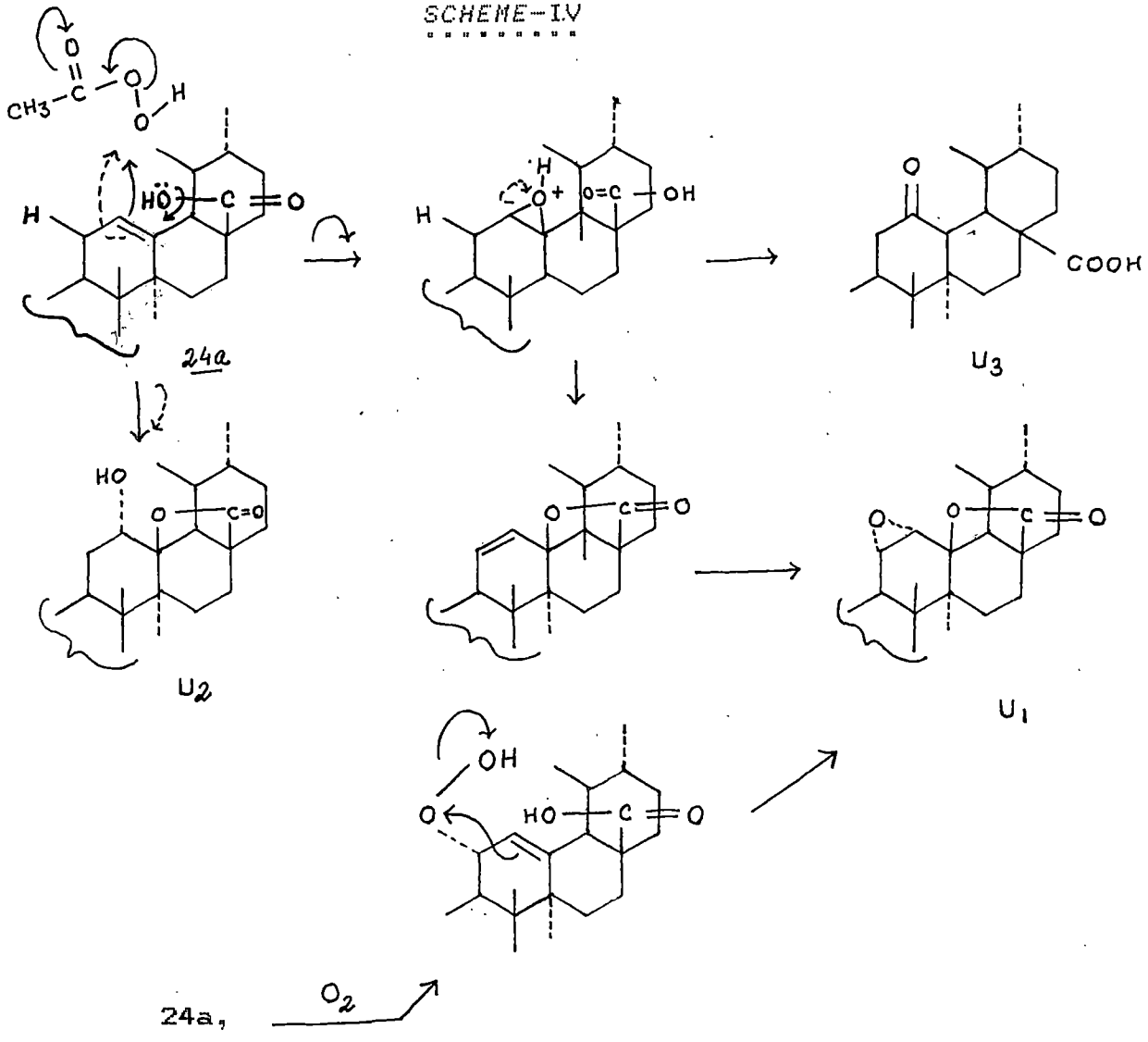


29a, R_1 = Ac, R_3 = H, R_2 = R_4 = Me,
29b, R_1 = Ac, R_2 = H, R_3 = R_4 = Me

30a, R_2 = H, R_1 = R_3 = Me
30b, R_1 = H, R_2 = R_3 = Me

Majumder et al[15] suggested the following mechanism for the formation of U_1, U_2, and U_3 as shown in Scheme IV

SCHEME-IV

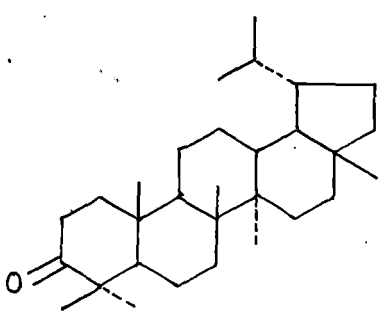


After isolation of products **29a**, **30a** and **26** from ursolic acid acetate **24a** the action of H_2O_2 in boiling acetic acid. Majumder et *al*[16] carried out this reaction to oleanolic acid acetate **24b** and isolated. epoxy γ-lactone **29b** and 12 hydroxy γ-lactone **30b** but keto dihydro derivative was absent. They[16] suggested that the presence of keto dihydro derivative **26** in case of **24a** and the absence of keto dihydro derivative in case of oleanolic acid acetate **24b** was due to the additional steric effect of 19-methyl group in **24a**.

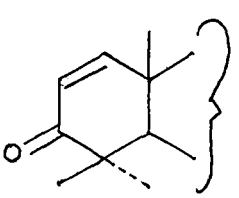
Based on the assumption that 17-CH_2OH group in the ursane and oleanane systems might undergo necleophilic participation like

17-carboxyl functions in this systems, Majumder et al[16] carried out H_2O_2-AcOH reaction with uvaol **24c** and erythrodiol **20**. In case of **24c** three products were 28-O-acetyl uvaol **24d**, 3-O-acetyl Uvaol **24e** and 3,28-O,O-diacetyl uvaol **24f**, similarly **20**, gave **24g**, **24h**, and **24i**. The total absence of any oxidation product in the reaction of **24c** and **20** with H_2O_2 -AcOH established the significant role played by the C_{17}- carboxyl group in initiating oxidative transformation of **24a** and **24b**. They [16] finally suggested that for any appreciable oxidation with H_2O_2 to be initiated by the 12,13-double bond in the ursane and Oleanane skeleta, *the presence of 17-carboxyl group was an essential requirement*.

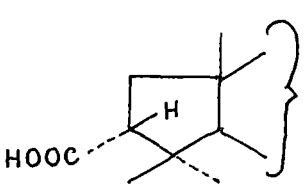
The SeO_2 catalysed reaction of H_2O_2 on pentacyclic triterpene 3-ketone was studied by Pradhan et al[17]. They[17] observed that lupanone **31** on oxidation with molar proporation of H_2O_2 and catalytic amount of SeO_2 in t-BuOH afforded lup-1-ene-3-one[19] **32**, 2α-carboxyl-A-nor-lupane[20] **33** and 2,3 seco-lupane dicarboxylic acid **34**; with excess H_2O_2 **31** furnished 4, 23,24 tri-nor-lupane 3 5 olide, a δ- lactone **35** together with [21] **34**



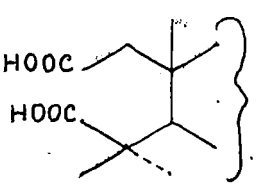
31,



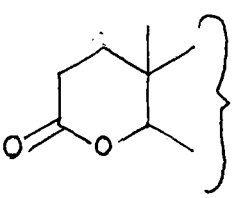
32,



33,



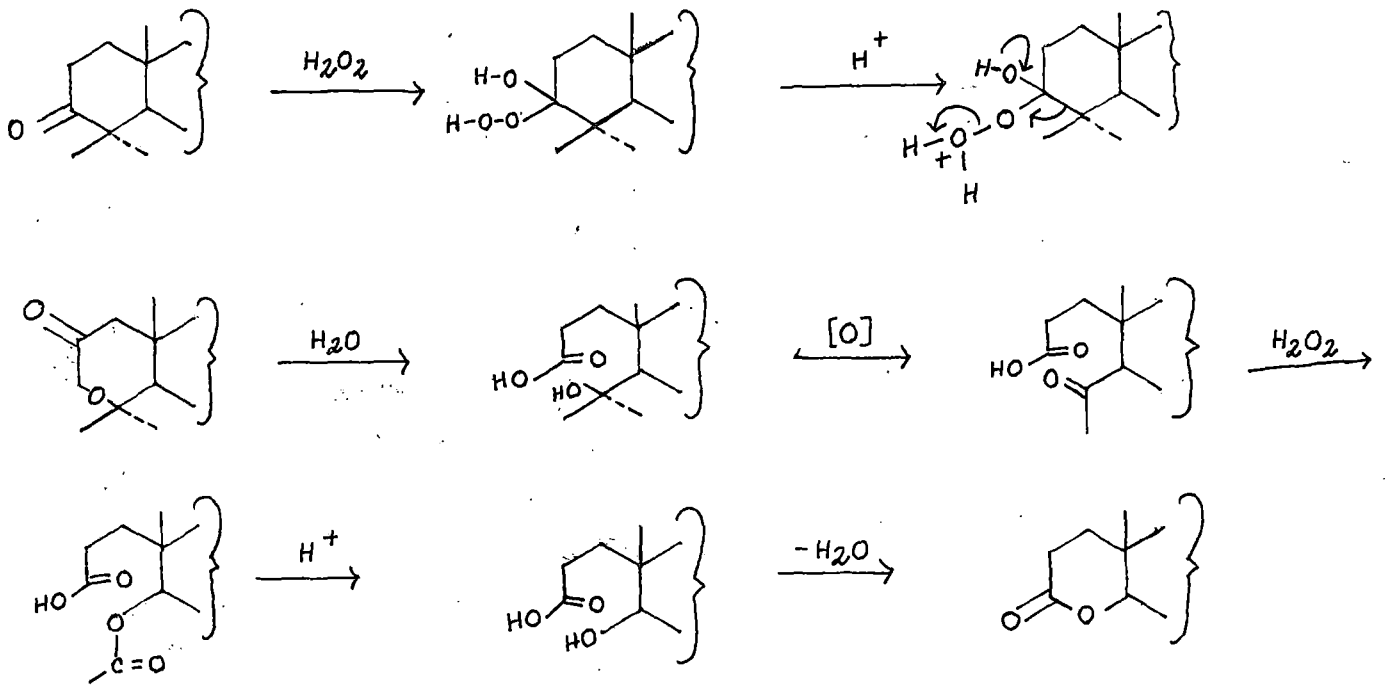
34,



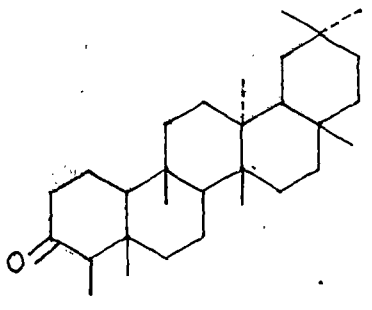
35,

Pradhan et al[17] suggested the following mechanism for the formation of δ-lactone 35 shown in scheme-V

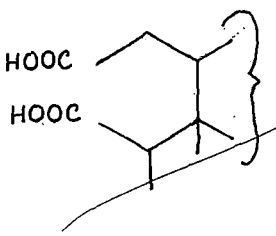
SCHEME-V



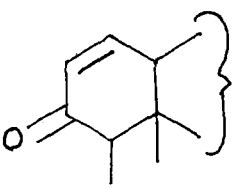
Pradhan et al[18] performed similar reactions of H_2O_2-SeO_2 in t-BuOH on friedlin 36 and reported the isolation of 2,3 seco-friedlinic acid 37, 2α- carboxy-A-nor-friedlin 38 and a δ-lactone.39.



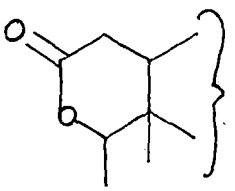
36.



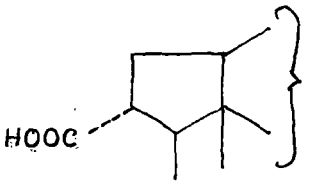
37.



36d.



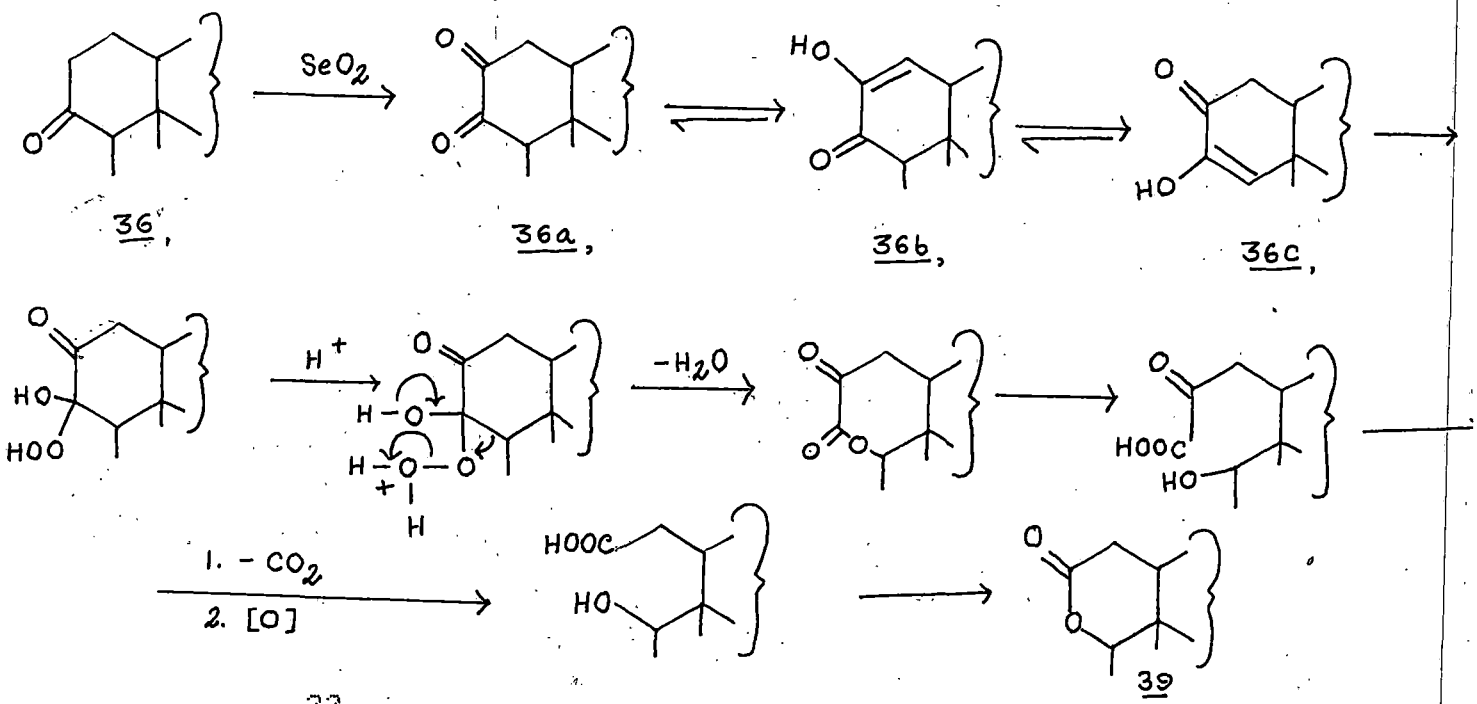
39



38

The mechanism suggested by Pradhan et al[18] shown in scheme-VI. They suggested that the formation of δ-lactone 39 proceeded via the formation of the diketone 36a [⇌ diosphenol ⇌ 36b ⇌ 36c]

SCHEME -VI

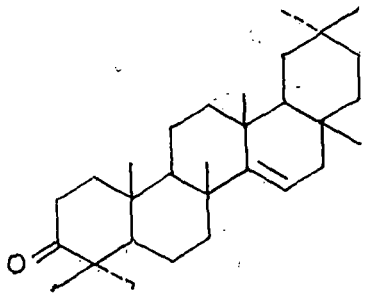


36, 36a, 36b, 36c, 39

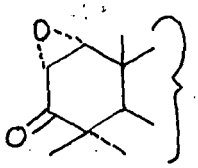
Anjaneyulu et al[22] reinvestigated the oxidation of friedlin 36 with H_2O_2-SeO_2 in t-BuOH and reported the formation of friedel-1-ene-3-one 36d and friedelolactone 39 along with 37 and 38 already reported by Pradhan et al[18].

Pradhan et al[23] extended the reaction to taraxerone 40,a 3-keto triterpenoid having a trisubstituted double bond. They[22] reported that 40 on oxidation with H_2O_2 in presence of SeO_2 in t-BuOH afforded 1α ,2α-epoxide 41, 4, 23, 24-tri-nor-taraxerene 3 5 olide, a δ- lactone 42 and taraxerene-ε-lactone 43 from neutral part and 2α-carboxyl-A-nor-taraxerene 44 together with taraxerene 3,4 seco-dicarboxylic acid 45 from acid part. The formation of the products 41,42,43,44,45 shows that in SeO_2 oxidation of taraxerone 40,no migration of 14-15 double bond took place. They concluded from previous studies and present observations that the δ-lactones were

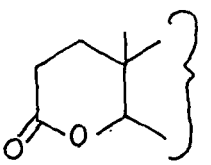
formed irrespective of the presence of methyl groups at C-4 position. Further isolation of ε-lactone 43 supported the mechanism of formation of δ-lactone via the ε-lactone. They also suggested that the epoxide 41 was most probably formed via Δ^{1-2} unsaturated ketone.



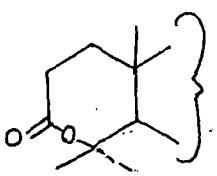
40,



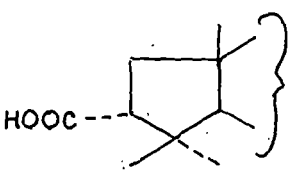
41.



42



43.



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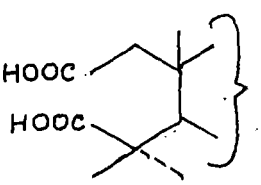
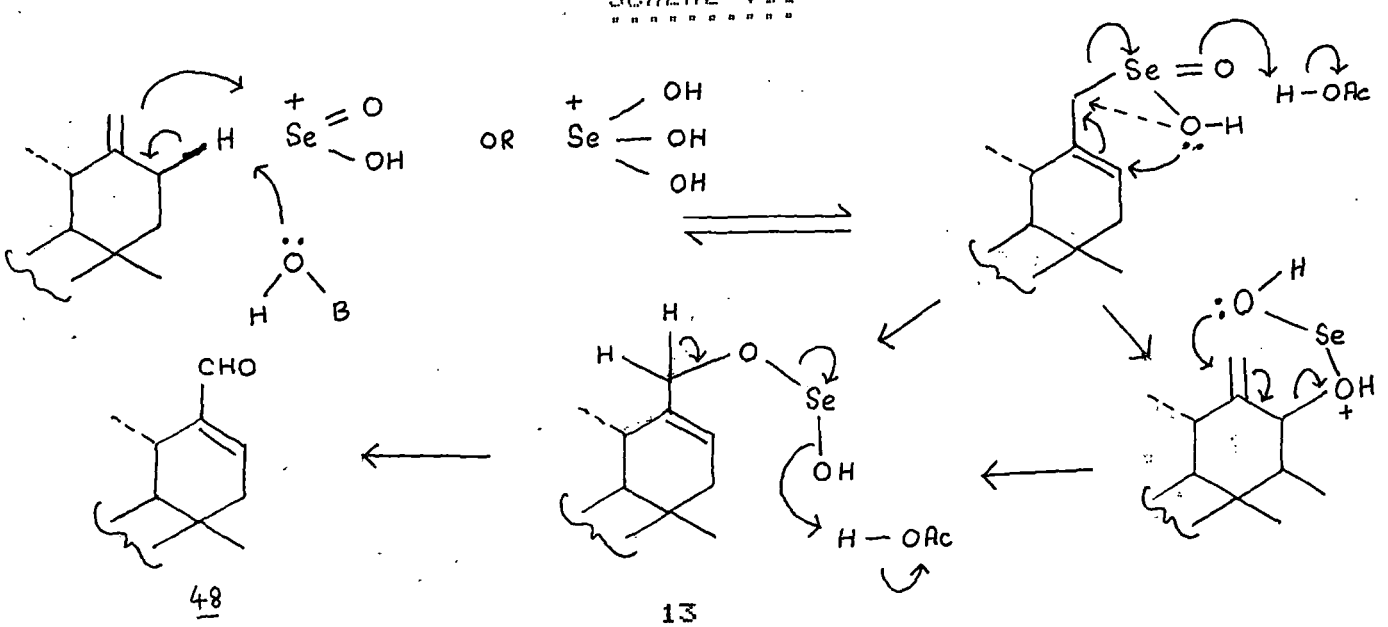


45.

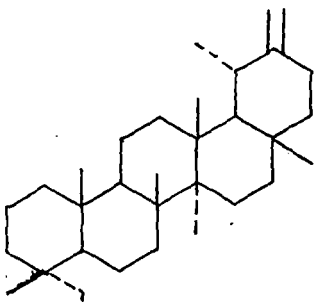
Talapatra et al[24] explained oxidation of taraxastene 46 and ψ-taraxastene 47 to give the corresponding aldehyde 48 on the basis of mechanism shown in scheme-VII

SCHEME-VII

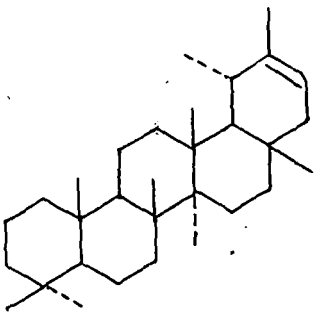


48

13

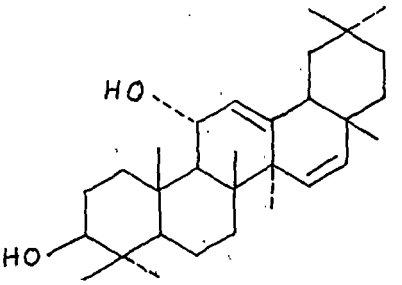


46,

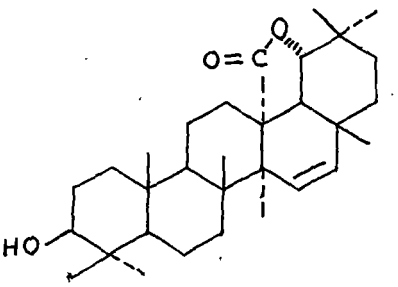


47,

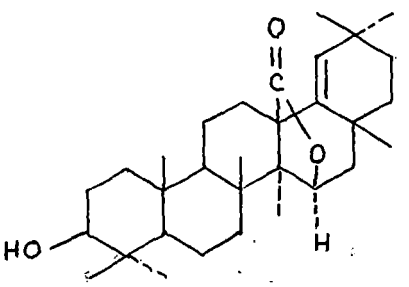
Pradhan et al[25] carried out the reaction of olean-12,15,dien 3,11-diol **48a** with H_2O_2 p-toluene sulphonic acid under identical condition of Corey et al[9] with a view to produce the multiflorenol derivative **51**. But they[26] isolated to isomeric γ-lactones identified as 3β-acetates of C_{12}-nor-olean-15(16)-en-13α-carb$\rightarrow$19α-olide **49** and C_{12}-nor-olean-18 (19)-en-13β-carb$\rightarrow$15β-olide **50**.



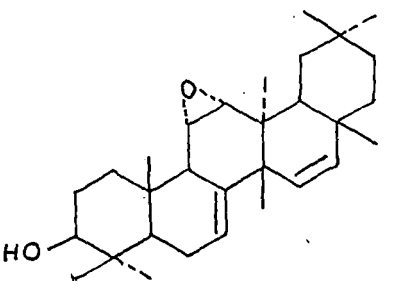
48a



49,

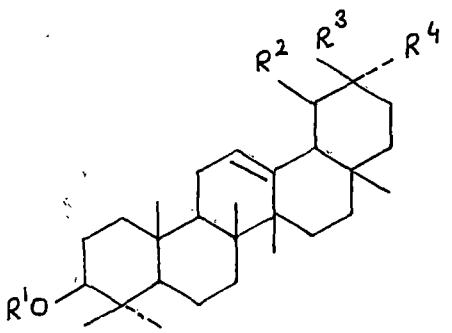


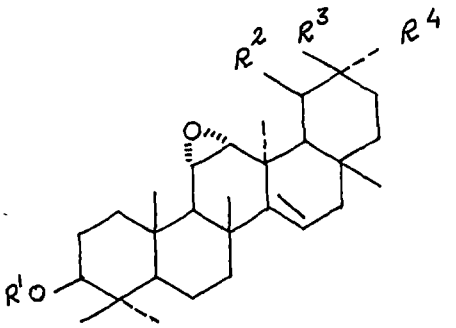
50,



51,

Pradhan et al[26] studied the reaction of SeO_2-H_2O_2 on β-amyrin acetate 51 in t-BuOH and reported two compounds as 11α,12α-epoxy-taraxer-14-en-3β-yl acetate 52 and 11α,12α-epoxy-taraxer-14-en-3β-ol 53 while on similar treatment, α-amyrin acetate 54 furnished 11α,12α-epoxy-urs-14-en-3β-yl acetate 55 and 11α,12α-epoxy-urs-14-en-3β-ol 56

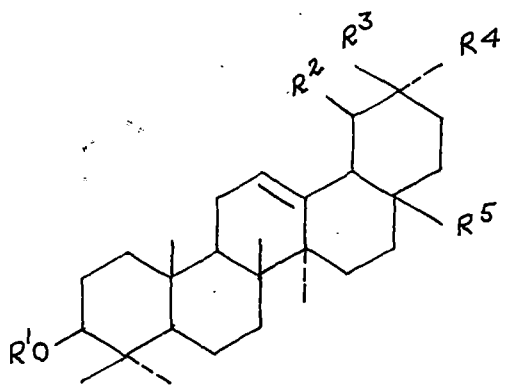


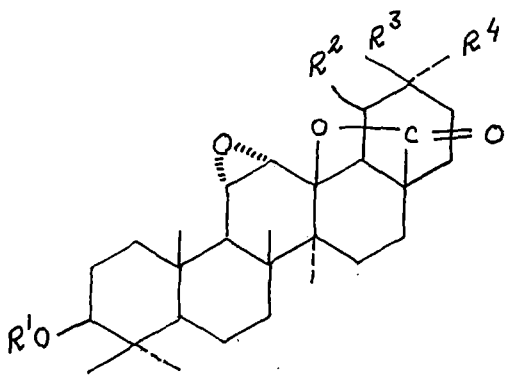


51, R^1=Ac, R^2=H, R^3=R^4=CH_3
54, R^1=Ac, R^4=H, R^2=R^3=CH_3

52, R^1= Ac, R^2= H, R^3=R^4=CH_3
53, R^1= R^2= H, R^3= R^4= CH_3
55, R^1=Ac, R^4= H, R^2= R^3=CH_3
56, R^1=R^4=H, R^2=R^3=CH_3

They[26] studied the action of SeO_2-H_2O_2 on acetyl oleanolic acid 57 and acetyl methyl oleanolate 58 in t-BuOH and isolated 11α,12α-epoxy-oleanan-28 13-olide-3β-yl acetate 59 and 11α,12α-epoxy-oleanan-28 13-olide 3β-ol 60. Under similar condition methyl acetyl ursolate 61 afforded two compounds identified as 11α,12α-epoxy-urs-28 13-olide -3β-yl acetate 62 and 11α,12α-epoxy-urs-28→13-olide-3β-ol 63.





57, R^1=Ac, R^2=H, R^3=R^4=CH_3, R^5=COOH

58, R^1=Ac, R^2=H, R^3=R^4=CH_3, R^5=$COOCH_3$

61, R^1=Ac, R^4=H, R^2=R^3=CH_3, R^5=$COOCH_3$

65, R^1=R^2=H, R^3=R^4=CH_3, R^5=CH_2OH

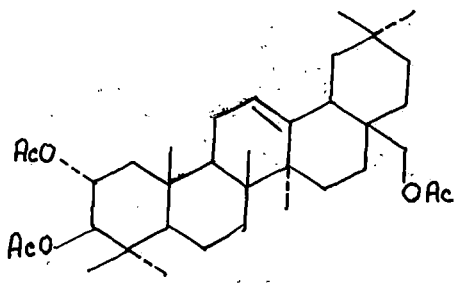
59, R^1=Ac, R^2=H, R^3=R^4=CH_3

60, R^1=R^2=H, R^3=R^4=CH_3

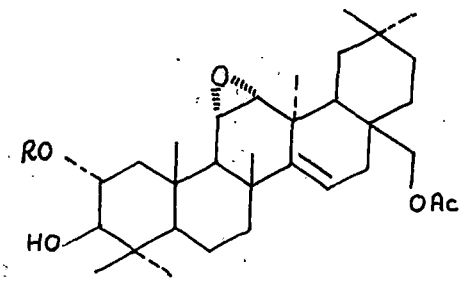
62, R^1=Ac, R^4=H, R^2=R^3=CH_3

63, R^1=R^4=H, R^2=R^3=CH_3

Pradhan et al[27] also carried out the reaction on erythrodiol **65** when the product **60** was formed whereas similar oxidation on the tri-acetate **66** furnished the epoxy derivatives **67** and **68** only.



66,



67, R = Ac

68, R = H

from these reactions they concluded:-

(1) the reaction is identical to the photochemical oxidation in the formation of 11,12, epoxide.

(2) the C-17 Carbomethoxy group as well as the CH_2OH group at the C-17 position is also involved in the formation of 28 13 lactone ring.

(3) the primary-CH_2OAc group at C-17 do not undergo hydrolysis where as the secondary -CHOAc group partially hydrolyses to -CHOH group under the reaction condition.

CHAPTER-II

This chapter has been divided into four sections from Section A to Section D.

SECTION-A.

Oxidation of triterpenoid ketones[17,18,22,27] with selenium dioxide or selenium dioxide in presence of hydrogen peroxide mixture in tertiary butanol have been reported. But there is no report on the studies of oxidation of triterpenoids having double bonds in ring-A containing 4,4-dimethyl system with selenium dioxide-hydrogen peroxide in tertiary butanol. So the author carried out some reactions of that type and the results of such oxidations are being reported in this section of the thesis.

OXIDATION OF 2,3-DEHYDRO-LUPANE 71 WITH SELENIUM DIOXIDE-HYDROGEN -PEROXIDE IN TERTIARY BUTANOL.

The product obtained after refluxing a solution of 2,3-dehydro-lupane in tertiary butanol with selenium dioxide containing hydrogen peroxide for 40 hours, was subjected to column chromatography for purification. On elution with benzene-chloroform (4:1) mixture a solid material was obtained which was crystallised from chloroform-methanol, *M.P.* 245-6°C. Its IR spectrum indicated the presence of hydroxyl group and hence it was acetylated with acetic anhydride-pyridine mixture and the product on column chromatography afforded a single compound-A on elution with benzene-petrol (2:3) mixture.

Characterisation of compound A :-

Compound A was purified by crystallisation from chloroform-methanol mixture, *M.P.* 221-2°C, $[\alpha]_D$ +23.4°. Its IR spectrum (fig.1) showed peaks at 1750, 1270 and 1250 cm^{-1} showing the presence of acetate function. Elemental analysis showed the molecular formula of A to be $C_{34}H_{56}O_4$ which is in agreement with its mass spectrum (fig.2). It showed molecular ion peak at m/e 528 (M, 86%)$^+$; the other fragments of prominence appeared at m/e 513 (M $-CH_3$, 30)$^+$, 485

$(M - C_3H_7, 43)^+$, 468 $(M - AcOH, 78)^+$, 408 $(M - 2X\ AcOH, 100)^+$, 393 (88), 365 (52.5), 231 (74), 191(86), 187(98), 123(94) . The ^1H NMR spectrum (fig.3) of compound A showed the presence of two secondary methyl groups that appeared as doublet centered at (δ in ppm.) 0.77 and 0.84 (J = 7 Hz.) respectively; the six tertiary methyl groups appeared as singlet (3H each) between 0.76 to 1.08; two singlets (3H each) that appeared at 2.01 and 2.07 were due to two acetoxy methyls (2 X $-OCOCH_3$). The doublet at 5.07 that coupled with vicinal proton with coupling constant of 7 Hz. was due to coupling between equatorial C-2α-H with equatorial C-3β-H which is geminal to the acetoxyl group. The double doublet that appeared at 4.96 with coupling constant 7 & 13 Hz. were due to C-2 proton that coupled with C-3β-H and C-1β-H which caused flatness of the peaks and the latter coupling was due to the coupling of C-2 proton with C-1 axial proton. The coupling constants and their positions are in agreement with the 2β,3α- diacetoxyl derivative of oleanane/lupane as reported in literature[28] shown in the table-I.

TABLE-I.

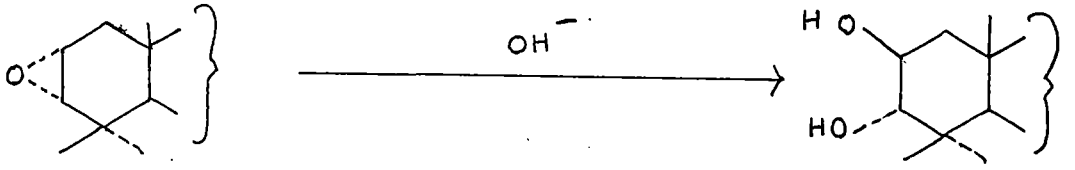
^1H NMR signals of methyl 2,3 dihydroxy Urs-12-en-28-oates and their diacetates with coupling constant in Hz. within parenthesis.

Assignments	2β,3α-$(OH)_2$,	2β,3α-$(OAc)_2$,	2β,3β-$(OH)_2$,	2β,3β-$(OAc)_2$
2-H	3.75 ddd (17, 10,2)	4.95 dd (13, 6.5)	4.08 ddd (4, 4,3)	5.31 ddd (4, 4,3)
3-H	3.63 d (10)	5.03 d (6.5)	3.20 d (4)	4.61 d (4)
Assignments.	2α,3β-$(OH)_2$,	2α,3β-$(OAc)_2$,	2α,3α-$(OH)_2$,	2α,3α-$(OAc)_2$.
2-H	3.68 ddd (11, 10, 4.5)	5.10 ddd (11,10.5,4.5)	4.00 ddd (12,4.5,3)	5.23 ddd (12,4.5,3)
3-H	2.99 d (10)	4.75 d (10.5)	3.43 d, (3)	4.96 d (3)

Thus compound A has been identified as lupan-2β,3α-diyl-acetate 73 and the original compound is therefore identified as lupan-2β,3α-diol, 72.

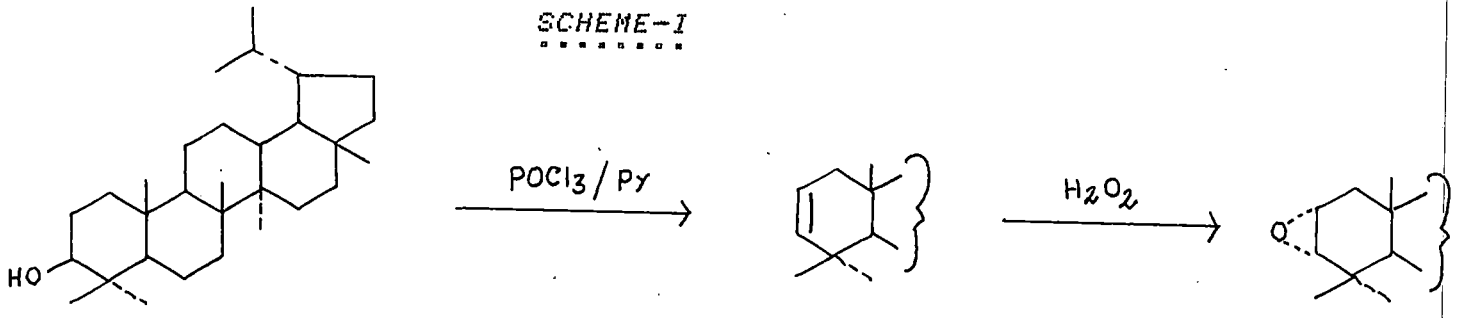
Mechanism for the formation of 2β,3α lupan-diol with selenium dioxide and hydrogen peroxide :-

The olefinic double bond at 2-3 position in ring-A of triterpenoids are much more less hindered than other position and hydrogen peroxide generally forms epoxide from the less hindered alpha side to furnish 2α,3α-epoxide. Under the acidic condition of selenic acid (P_H = 4.2) the epoxide ring cleaves to furnish the *trans* diaxial product.



The formation of such trans diol with hydrogen peroxide-formic acid etc. from cyclic olefins are well known. The formation of 73 from lupanol 69 is schematically represented in scheme-I below :-

SCHEME-I



69 70 71

72. 73

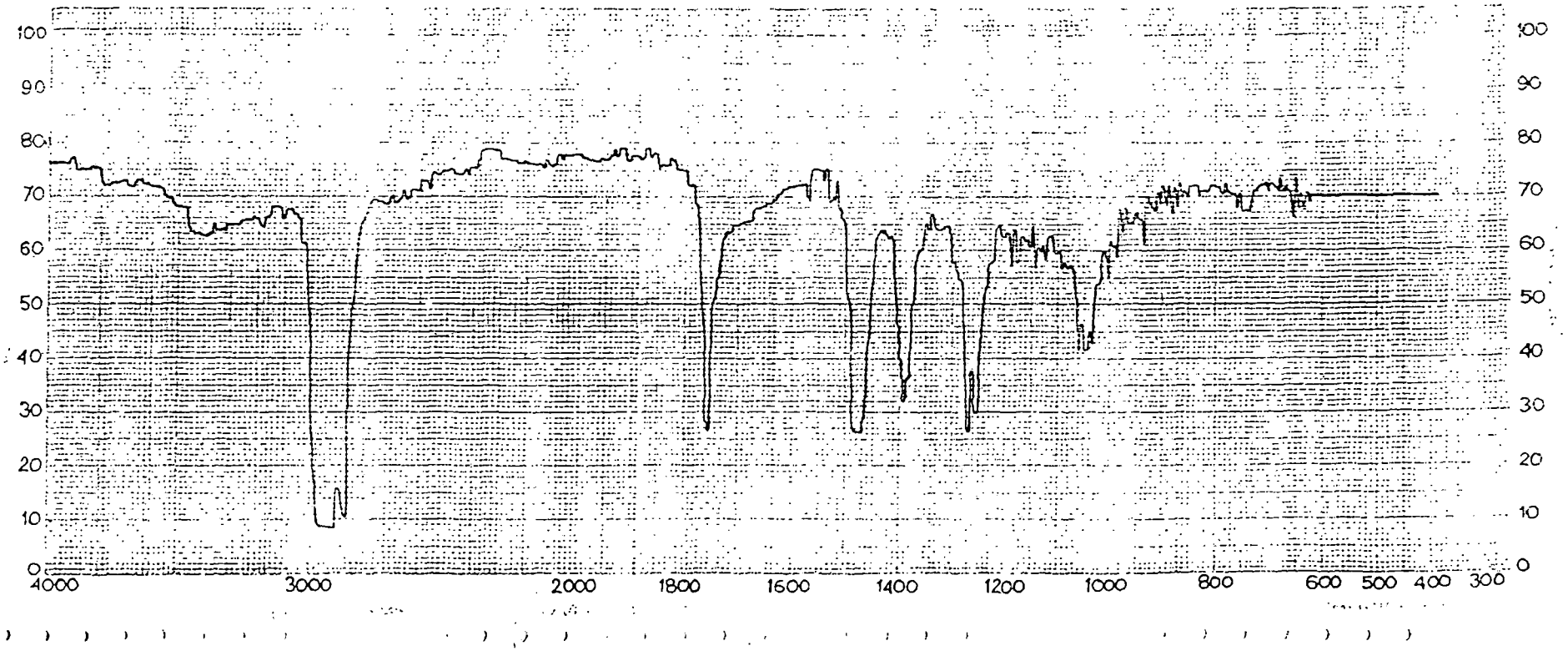


Fig. 1 : IR spectrum of lupan 2β,3α-diyl acetate, 73.

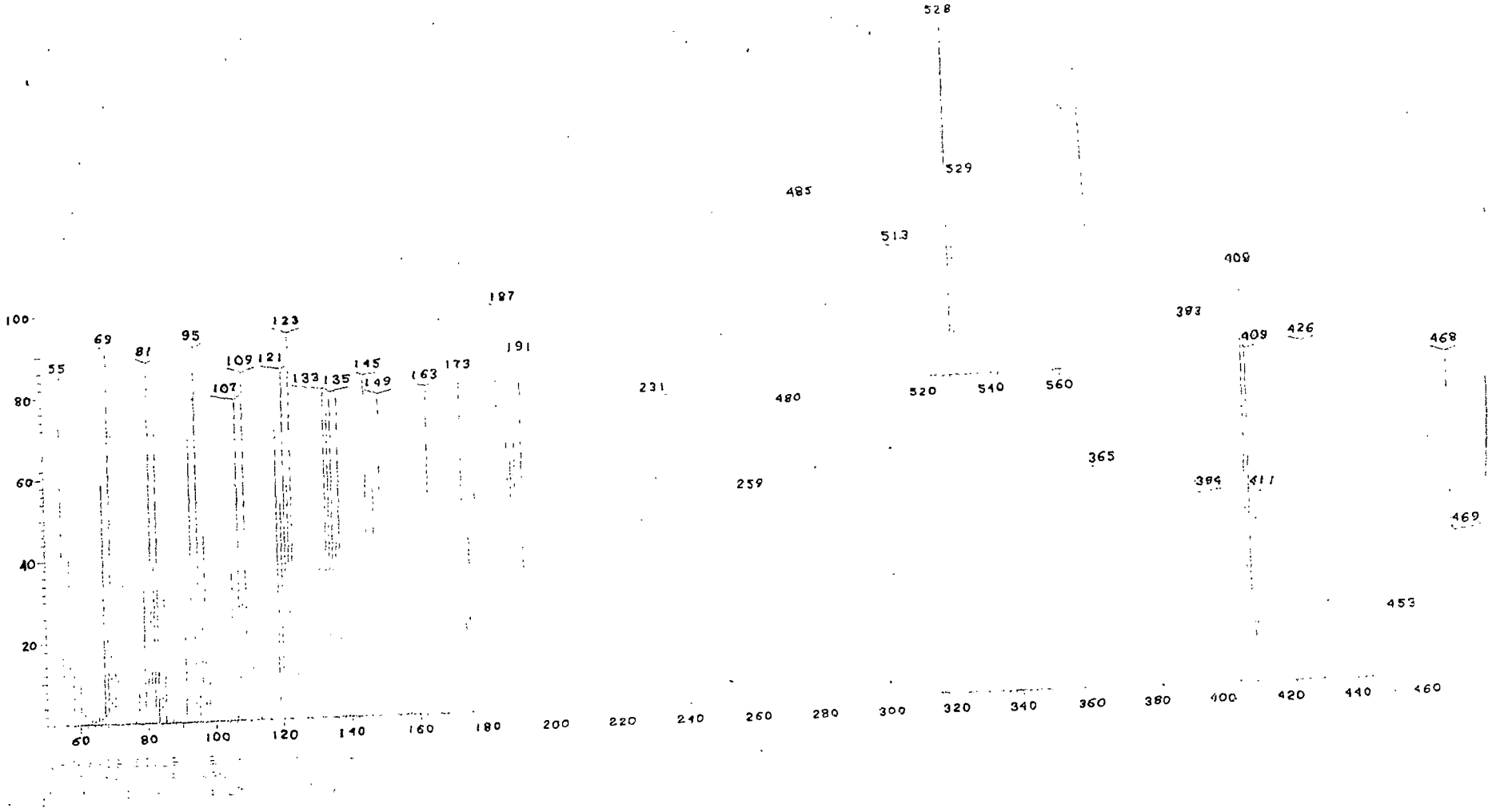


Fig. 2 : Mass spectrum of lupan 2β.3α-diyl acetate. 73.

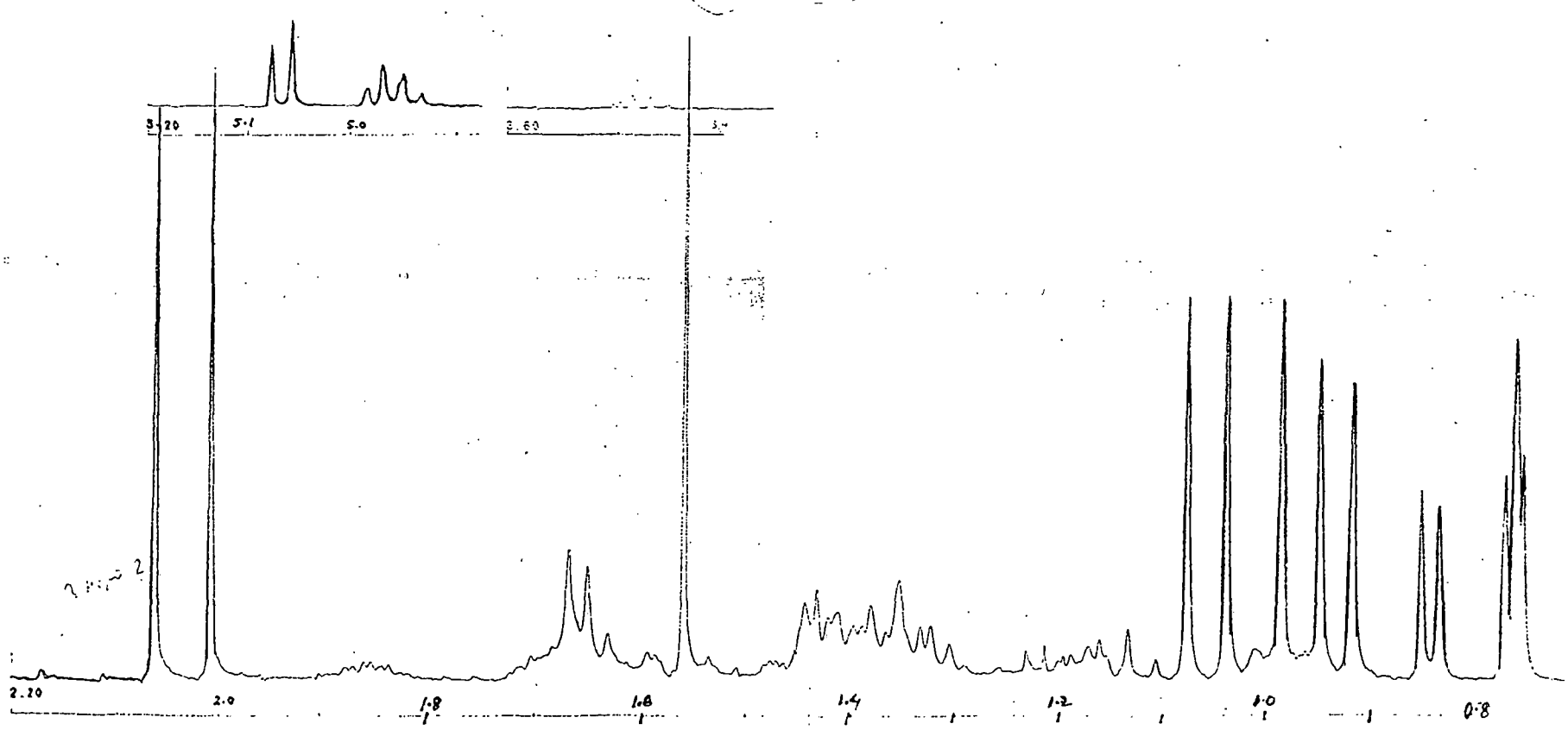


Fig. 3 : ^{1}H NMR spectrum of lupan 2β.3α-diyl acetate, 73.

OXIDATION OF 2,3-DEHYDRO-METHYL-DIHYDRO-BETULINATE 77 WITH SELENIUM-DIOXIDE IN TERTIARY BUTANOL CONTAINING HYDROGEN PEROXIDE.

The compound 2,3-dehydro-methyl-dihydro-betulinate was refluxed with selenium dioxide in tertiary butanol containing hydrogen peroxide for 40 hours over water bath. After usual workup the crude product was acetylated (as the IR spectrum showed the presence of hydroxyl group) with acetic anhydride-pyridine mixture and the product on subsequent chromatography afforded a single compound B on elution with petrol-benzene (1:4).

Identification of compound-B :-

Compound B was purified by repeated crystallisation from chloroform-methanol mixture yielding needle shaped crystals, *M.P.* 209-10^{0}C. The IR spectrum (fig.4) showed peaks at 1730,1710 cm^{-1} due to C=O stretching vibration of ester and acetate groups and 1230, 1220 cm^{-1} for -C-O- stretching vibrations of the same two functions.

Elemental analysis indicated the molecular formula to be $C_{35}H_{56}O_6$. Its mass spectrum (fig.5) showed molecular ion peak at m/e 572 (M, 4%)$^{+}$; the other fragments of importance appeared at m/e 512 (M - AcOH, 18)$^{+}$, 470 (M -[AcOH + C_3H_7],20)$^{+}$, 452 (M - 2x AcOH,68)$^{+}$ 437 (44), 411 (18), 393 (20), 377 (35), 203 (46), 191 (95), 187 (100).

From the mass spectrum and elemental analysis the molecular formula was confirmed to be $C_{35}H_{56}O_6$.

The ^{1}H NMR spectrum (fig.6) with different signals are recorded below in tabular form.

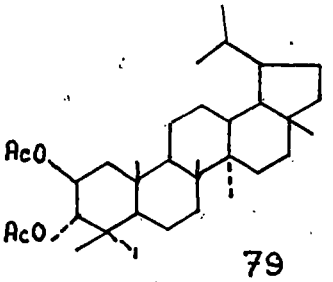
TABLE-II.

Chemical shift. (δ in ppm.)	Number of protons.	Multiplicity of signals.	Probable assignments.

0.74	3	doublet	CH_3-CH-CH_3
0.85	3	J = 7 Hz.	
0.90	2x3	singlet.	five
0.95	3	"	tertiary
0.96	3	"	methyl
1.05	3	"	groups.
2.01	3	singlet.	2x -O-CO-CH_3.
2.05	3	"	
3.64	3	singlet.	-CO-O-CH_3.
4.76	1	double doublet. J = 13, 7 Hz.	Ac-O-C_2-α H.
5.06	1	doublet. J = 7 Hz.	Ac-O-C_3-β H.

The ^{1}H NMR signals of compound B with those diacetate derivative of isomeric 2,3-diols of Oleanane and Ursane skeleton are presented in table-I in Section A for comparison.

From the spectral studies the structure of compound B is proposed to be 2β,3α-diacetoxy methyl dihydro betulinate 79.



79

The mechanism of the reaction is proposed to be same as suggested for 2,3 dehydro lupane in section-A of this chapter.

Thus, *it may be concluded that oxidation of olefinic double bond at C-2(3) position in ring-A of triterpenoids with selenium dioxide containing hydrogen peroxide exclusively produce 2β,3α - diols.*

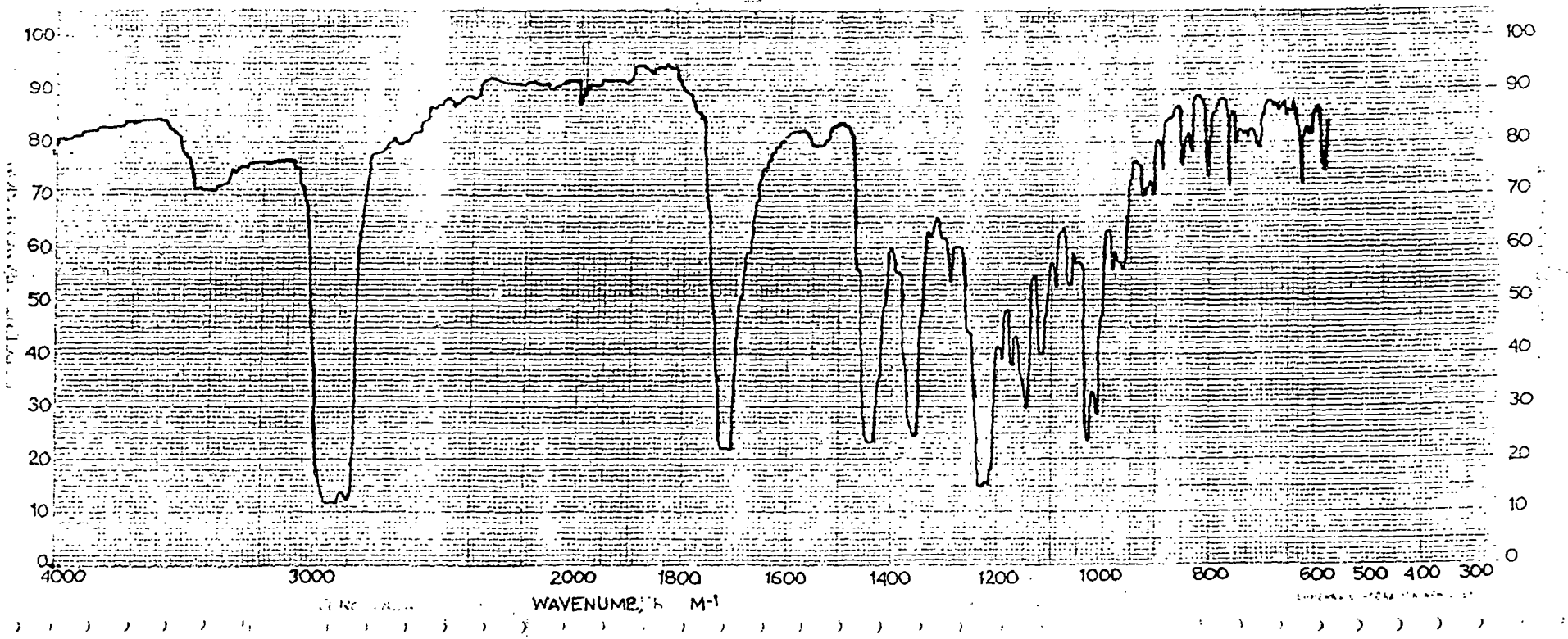


Fig. 4 : IR spectrum of 2β,3α-diacetoxy methyl dihydro betulinate 79.

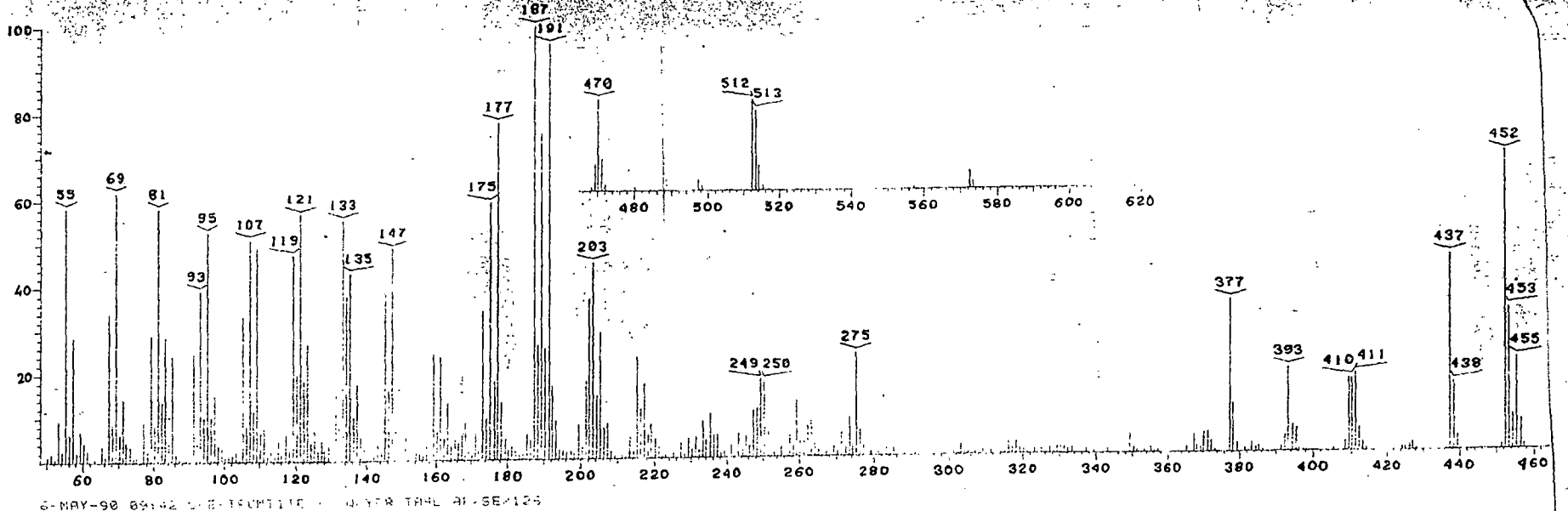


Fig. 5 : Mass spectrum of 2β,3α-diacetoxy methyl dihydro betulinate 79.

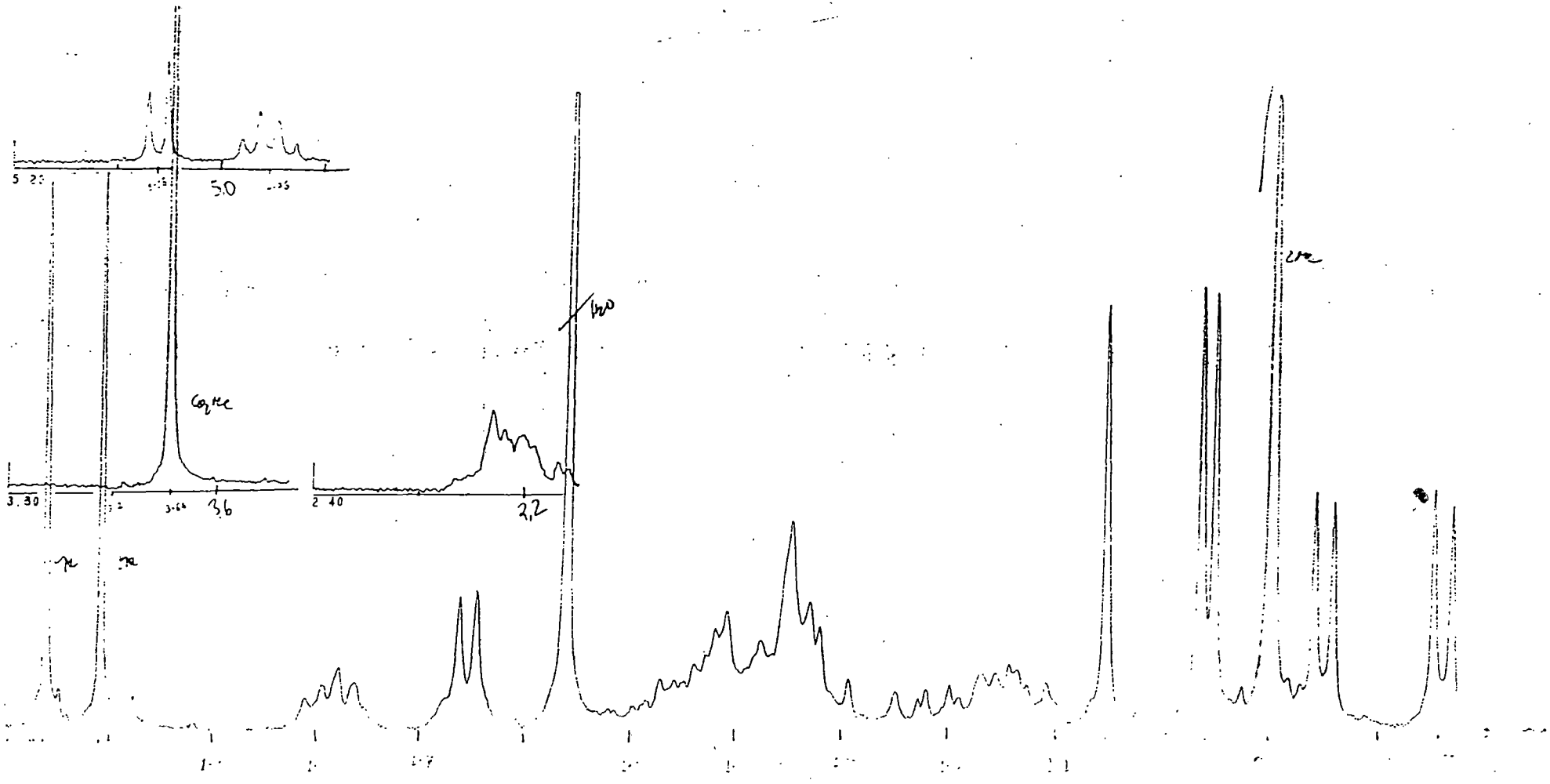


Fig. 6 : ^{1}H NMR spectrum of 2β,3α-diacetoxy methyl dihydro betulinate 79.

OXIDATION OF FRIEDEL-3(4)-ENE 82 WITH SELENIUM DIOXIDE-HYDROGEN PEROXIDE IN TERTIARY BUTANOL.

The products formed by oxidation of 2,3 dehydro lupane and 2,3 dehydro methyl dihydro betulinate with selenium dioxide in presence of hydrogen peroxide in tertiary butanol encouraged the author to extend the reaction on friedel-3(4)-ene and 3,4 dehydro friedelan 27->15α olide having 4-mono methyl system in ring-A.

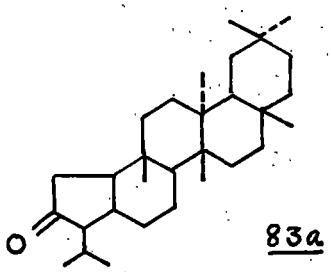
Oxidation of friedel-3(4)-ene:

Friedel-3(4)-ene 82 was refluxed with a mixture of selenium dioxide-hydrogen peroxide in tertiary butanol and the product obtained after usual work up was subjected to column chromatography - two different compounds C and D were obtained on elution with petrol-benzene (3:2) and benzene-chloroform (4:1) respectively.

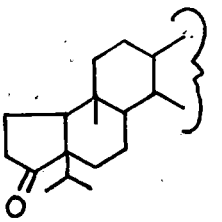
Characterisation of compound C :-

The compound C was crystallised three times from chloroform-methanol mixture to afford colourless crystals, *M.P.*207-8°C $[\alpha]_D$= +16°. In its IR spectrum (fig. 7) the presence of an absorption peak at 1715 cm^{-1} indicated that a ketone function in a six membered ring is introduced in the molecule by the reaction but the absence of absorption in the region 3200-3600 cm^{-1} showed that no hydroxyl group is formed in contrary to our previous observation. Moreover, the mass spectral and elemental analysis showed that an oxygen atom has been introduced in the molecule C making the molecular formula, $C_{30}H_{50}O$. The mass spectrum (fig.8) showed the molecular ion at m/e 426 $(M,14\%)^+$ with other fragments appearing at m/e 411 ($M-CH_3$, 12)$^+$,383 ($M-C_3H_7$, 20)$^+$, 355 (4.5),206 (21),205 (36),163 (27), 109 (38), 107 (100). The ^1H NMR spectrum (fig.9) showed presence of two secondary methyl groups centred at (δ in ppm.) 0.75 and 0.83; six other methyls as singlet in the region 0.75 to 1.07; two multiplets centred at 1.88 and 2.44 integrated for one proton each were due to α-protons to the carbonyl group which have β-protons to give multiplets. It is surprising to note that the reaction product C has two secondary

methyls which are probably in the form of isopropyl groupings. There is a gem dimethyl group as evident from the IR absorption at 1380, 1355 $cm.^{-1}$ Since the double bond is in 3(4)-position in ring-A and a ketone and isopropyl groupings are formed by the oxidising reagents, the formation of compound C having structure **83a** or **83b** could be assumed.



83a



83b

However, the structure **83a** posses a proton at C-3 carbon that would give a double doublet and the total number of α-proton to the carbonyl group would be three which is not observed. Moreover, the formation of isopropyl group at C-3 position with migration of C-5 methyl to C-4 with subsequent hydrogen addition seem to be rather difficult.Further, the fragmentation pattern of C do not follow the B:E friedelo-oleanan skeleton type.

The second possible product **83b** contains the isopropyl group at the C-5 position and the structure could explain most of the resonance peaks observed in the ^{1}H NMR spectrum of compound C. However,it may be noted that the methyl protons of the isopropyl group should appear down field due to the anisotropic effect of the nearby carbonyl group, whereas in the case of compound C this proton appear quite upfield at 0.75 and 0.83.Further, had there been any change in ring-A keeping other methyls at their original position then the protons at C-25,C-26,C-27,C-28,C-29 and C-30 should appear at positions almost same as in the case of friedelin. A comparison of the resonance peaks (δ in ppm.) of various methyl groups of compound C with that of friedelin is given in the table-III.

TABLE-III [29]

	C-23,	C-24,	C-25,	C-26,	C-27,	C-28,	C-29,	C-30.
friedelin (δ):	0.87	0.72	0.86	0.99	1.04	1.16	0.94	0.99
compound C (δ):	1.07	1.02	0.93	1.07	0.94	0.76	0.83	0.75

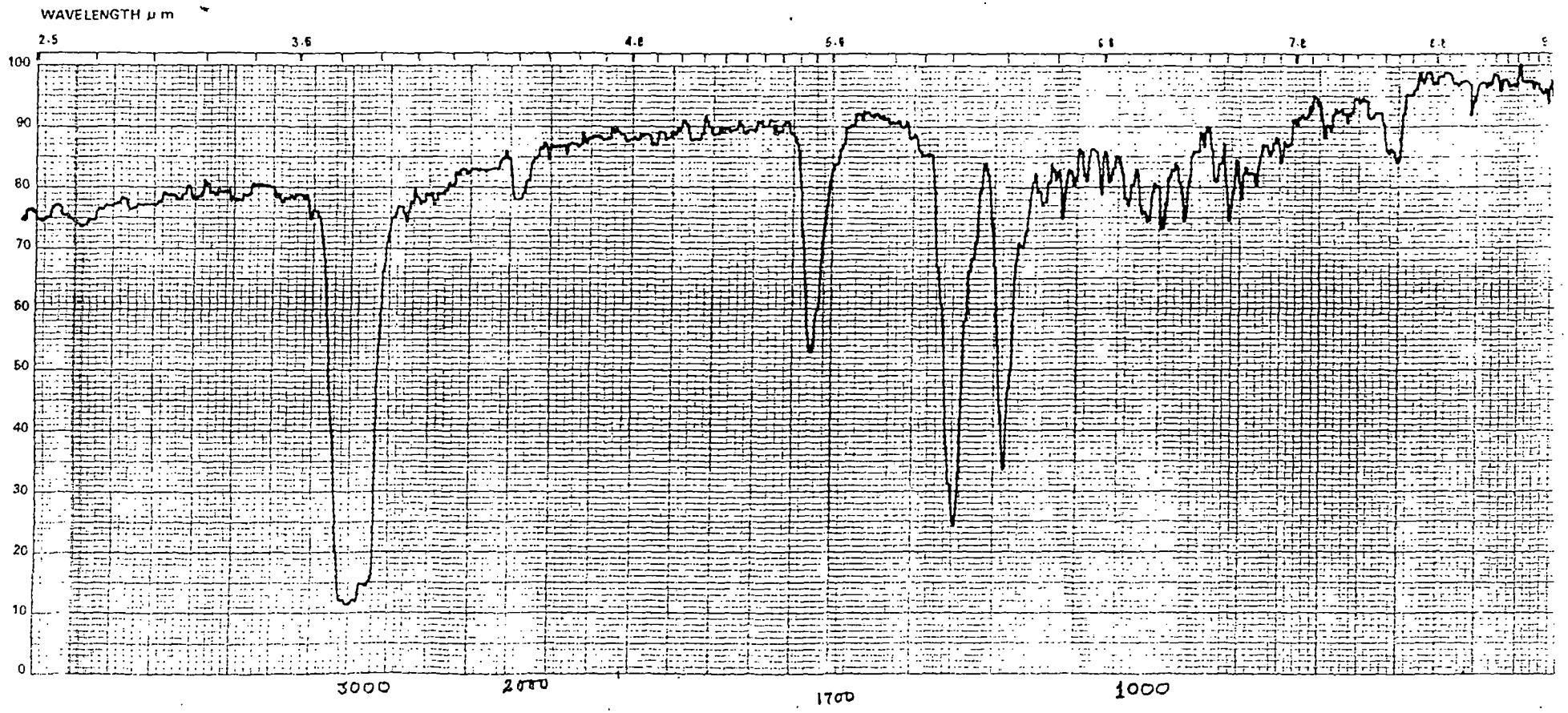


fig. 7 : IR spectrum of compound C. 83.

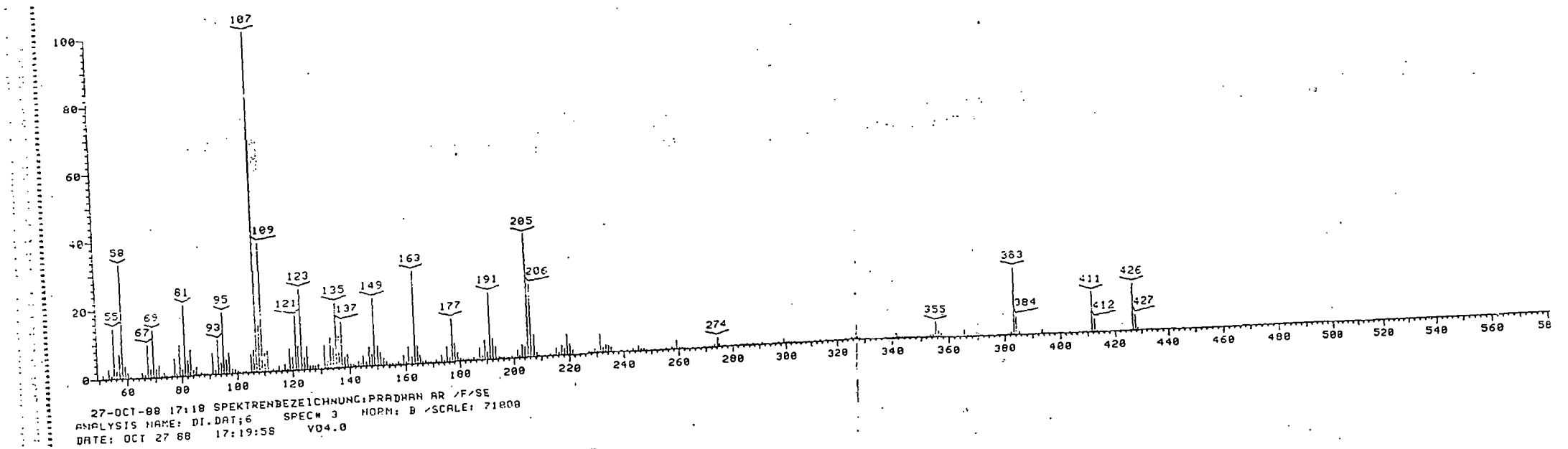


fig. 8 : Mass spectrum of compound C. 83.

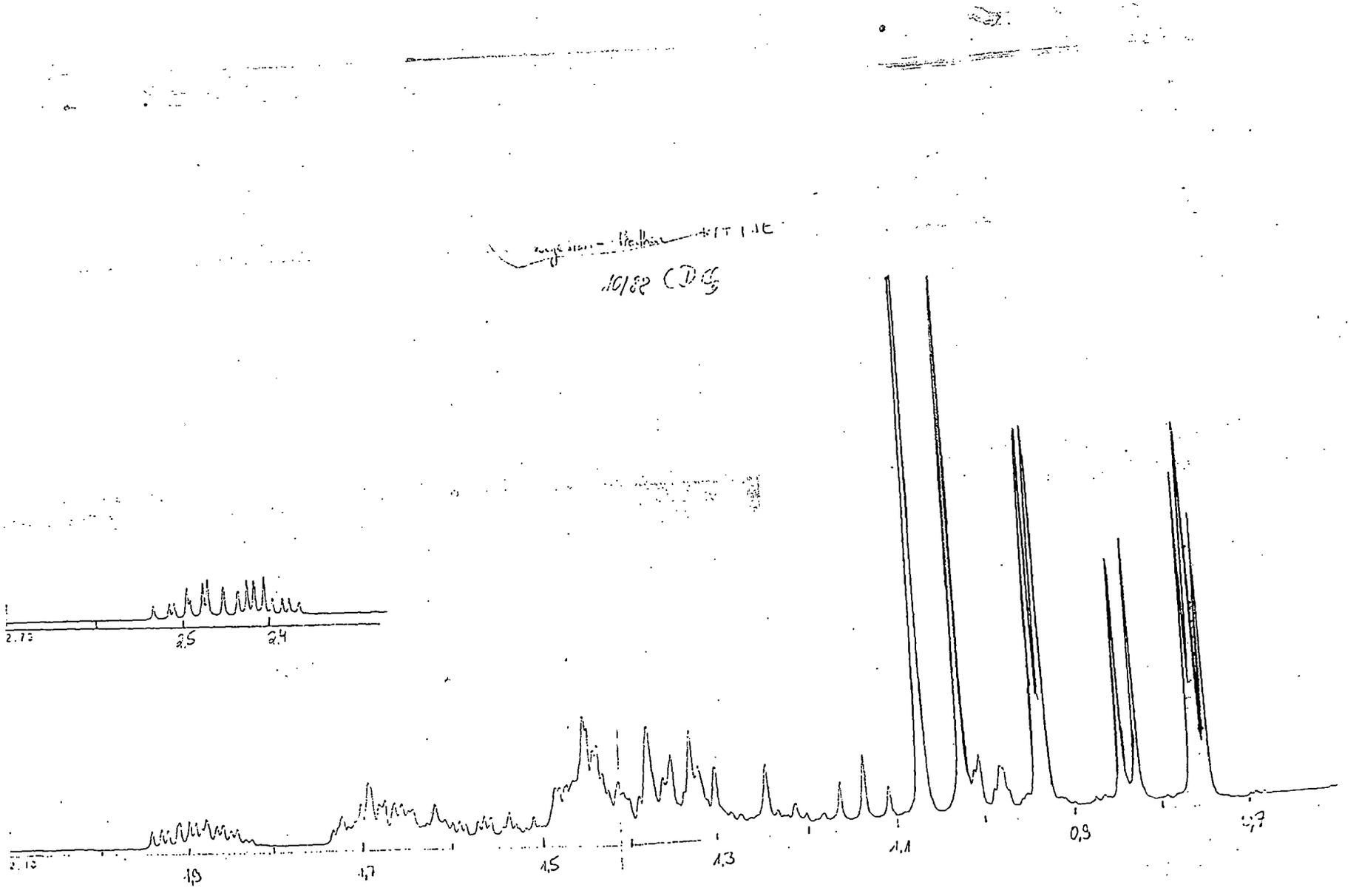


fig. 9 : ^{1}H NMR spectrum of compound C, 83.

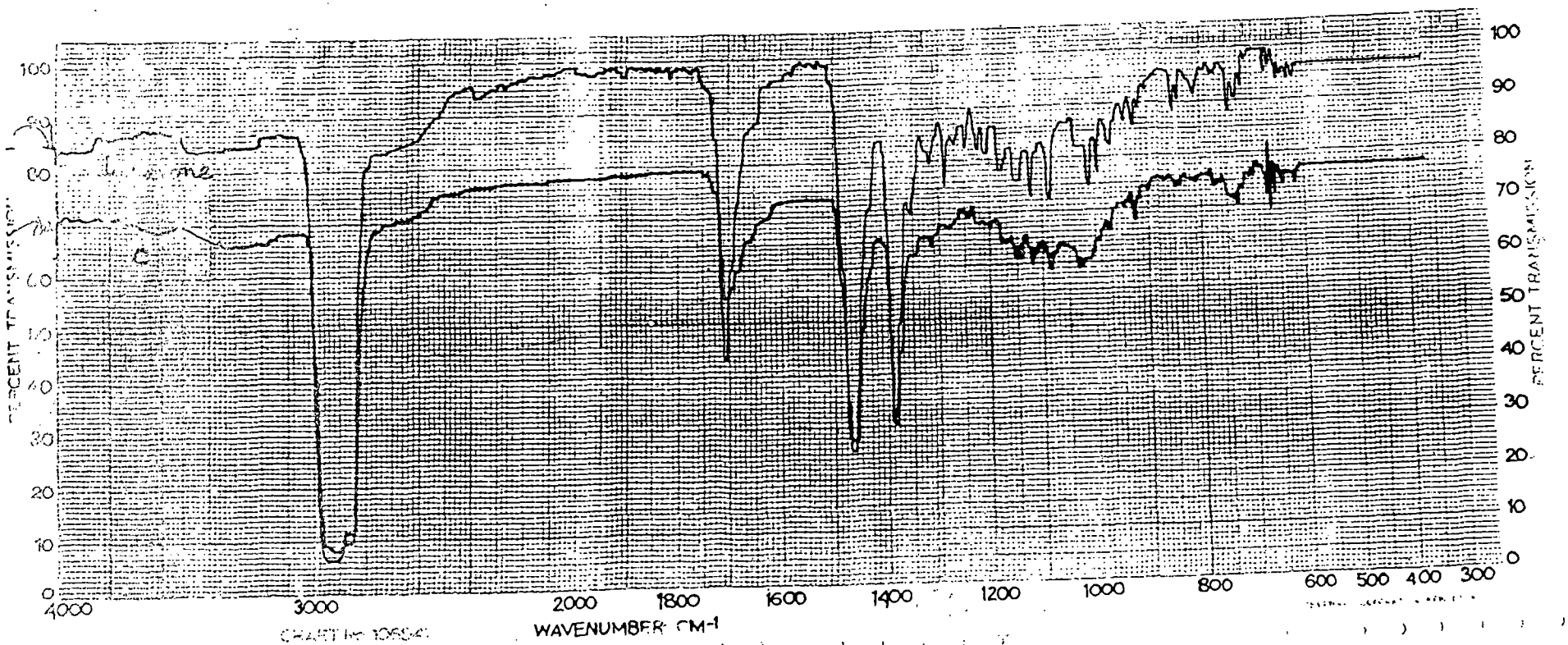


fig. 10 : Co-IR spectrum of compound C and lupanone.

The above comparison shows that compound-C is most probably having a skeleton other than friedelin.

This observation is further supported by the fact that the mass spectral fragmentation pattern of compound C do not follow the pattern of friedelane skeleton as mentioned in the foregoing statement.

A survey of literature on the fragmentation pattern of various saturated triterpenoid ketones revealed that lupanone exhibits the identical fragmentation pattern[30] with that compound C.

Compound C :	m/e	426	411	383	205	191
Lupanone :	m/e	426	411	383	205	191

A comparison of ^{1}H NMR datas of compound C with lupanone, lupenone, and lupane are given below in table-IV. Its identity was further confirmed by comparison with authentic sample of lupanone (*M.M.P.*, co-tlc,co-IR and ^{1}H NMR).

TABLE-IV.

^{1}HMR comparison of lupenone, lupane, lupanone and compound C.

Methyl group	23	24	25	26	27	28	29	30.
lupenone[36]	1.03	0.98	0.95	1.06	0.98	0.80	-	-
lupane[37]	0.84	0.78	0.83	1.03	0.93	0.76	0.84	0.76
Lupanone	1.07	1.03	0.94	1.07	0.95	0.77	0.84	0.76
Compound C	1.07	1.02	0.93	1.07	0.94	0.76	0.83	0.76

Hence, compound C is identified as lupanone **83**.

Identification of compound D :-

The compound D was crystallised from chloroform-methanol to afford white crystals, *M.P.* 235-6^{0}C, $[\alpha_D]$= +14.1^0,IR spectrum (fig.11) showed two peaks at 3340,3380 cm^{-1}indicating the presence of two hydroxyl groups; Its mass spectrum (fig.12) gave molecular ion paek at m/e 444 (M,72%)$^+$; other peaks were at m/e 429 (M-CH_3, 18)$^+$, 426 (M-H_2O, 30)$^+$,411 (10), 341 (12), 273 (14), 218 (32), 205 (57),163 (100).

From mass spectrum and elemental analysis the molecular formula is established to be $C_{30}H_{52}O_2$.

The ^{1}H NMR spectrum (fig.13) showed eight singlets in the region (δ in ppm.) from 0.88 to 1.25 for eight tertiary methyl groups; a

single proton that appeared as AB quartet centred at 3.56 with J_{ea} = 7 Hz. and J_{ee} = 3 Hz. showing that the proton is having two neighbouring protons with equatorial-equatorial and equatorial-axial coupling. Hence, the proton is equatorially oriented at C-3 and the hydroxyl group is axially oriented. The absence of a secondary methyl group and the existence of a tertiary methyl group downfield at 1.25 showed that the second hydroxyl group is attached to the C-4 position. Thus, the compound D could be friedelan 3β,4α diol. A survey of literature showed sengupta et al[31] prepared friedelan 3β,4α diol **84** using per-chloric acid as oxidising agent on friedelan 3α,4α epoxide **82a**.

Acetylation of compound D :-

Compound D **84** on acetylation with acetic anhydride-pyridine mixture gave a crystalline compound E **85**, *M.P.*245-6°C, $[\alpha]_D$ = 24°; IR spectrum showed absorption at 3500 cm^{-1} for hydroxyl group and 1720, 1280 cm^{-1} indicating acetate function. The mass spectrum showed molecular ion peak at m/e 486 (M)$^+$; other peaks were found at m/e 471, 444, 422, 408, 341, 333, 291,273, 260, 255, 247, 229, 205 (100%). The ^{1}H NMR spectrum of compound E showed eight singlets (3H each) between (δ in ppm.) 0.9 to 1.3 for eight tertiary methyl groups; a singlet appeared at 2.1 (3H) for acetate protons and the triplet that appeared at 4.75 (J = 3Hz.) is due to the methine proton that coupled with neighbouring protons and attached to the carbon atom bearing the acetate group.The inert character of the second hydroxyl group towards acetylating agent showed its attachment at the tertiary carbon (C-4). Hence, the possible structure of compound E is **85**.

The compound D on oxidation with Jones reagent gave compound E **86**, *M.P.* 253-4°C. IR spectrum (fig.**14**) showed absorption at 3470 cm^{-1} for hydroxyl group and 1715 cm^{-1} due to ketone function. Its mass spectrum (fig.**15**) showed molecular ion peak at m/e 442 (M, 10%)$^+$; other fragments of prominence appeared at m/e 436, 422, 407, 365, 281, 239, 211, 146, 111, 97, 85, 71, 57 (100). Thus, from the Mass and elemental analysis the molecular formula of compound E is found to be $C_{30}H_{50}O_2$.
^{1}H NMR spectrum (fig.**16**) of compound E showed seven singlets (3H

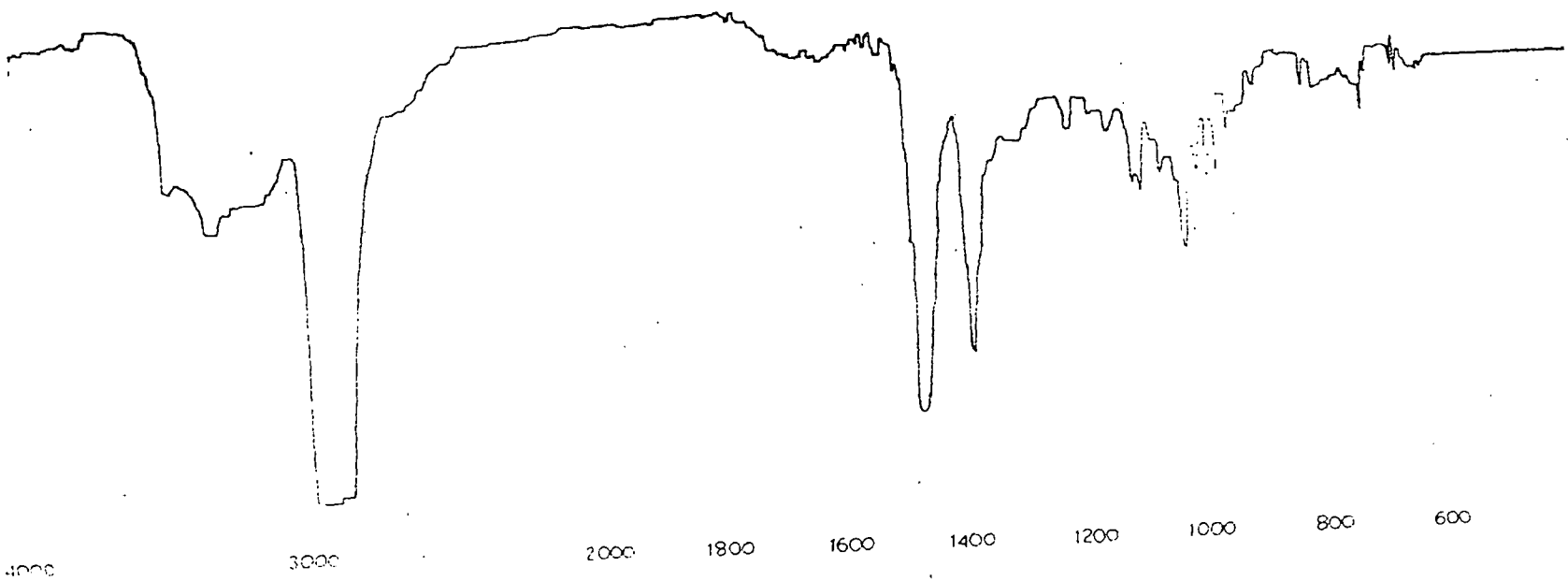


fig. 11 : IR spectrum of friedelan 3β,4α-diol, 84.

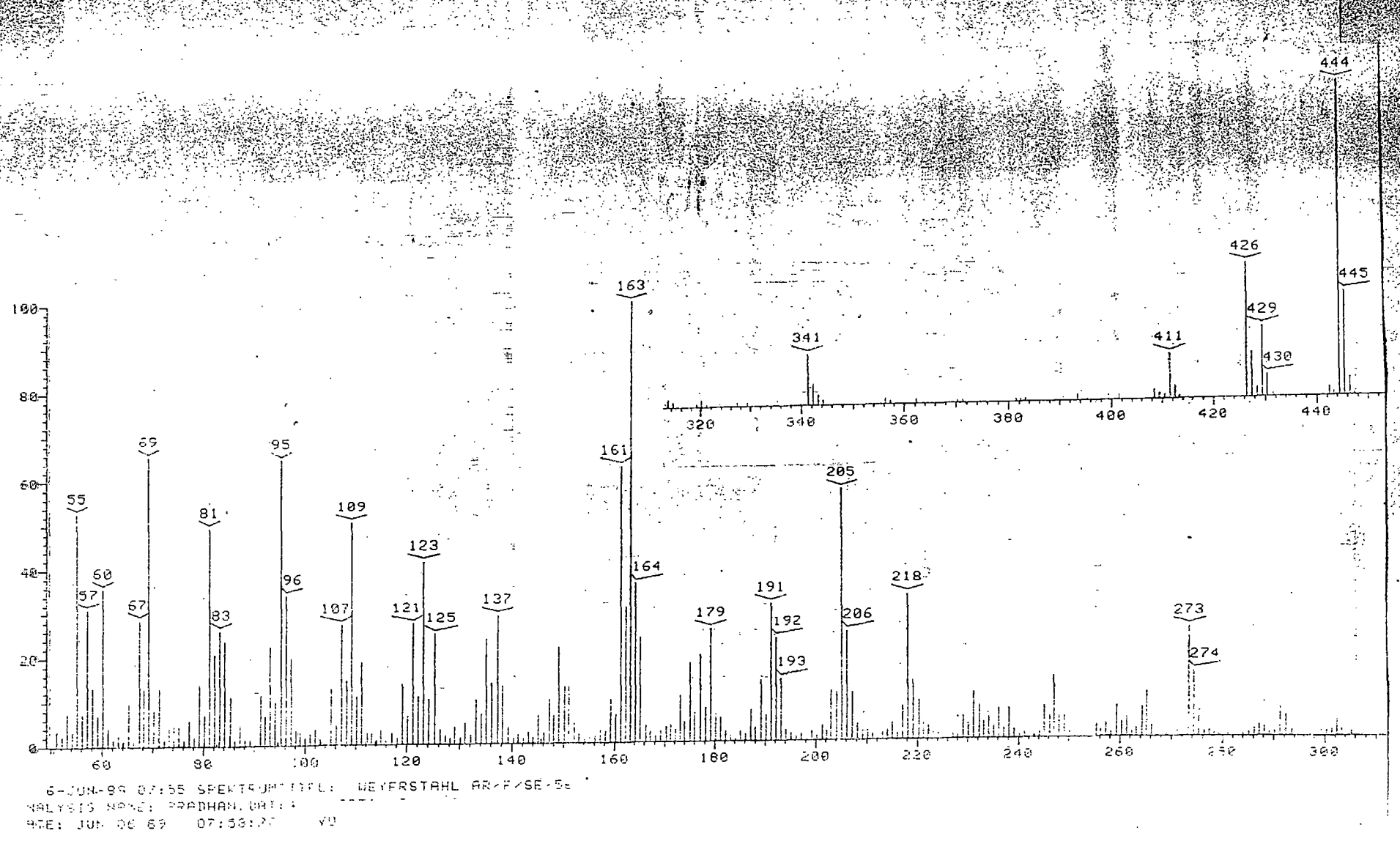


fig. 12 : Mass spectrum of friedelan 3β,4α-diol, 84.

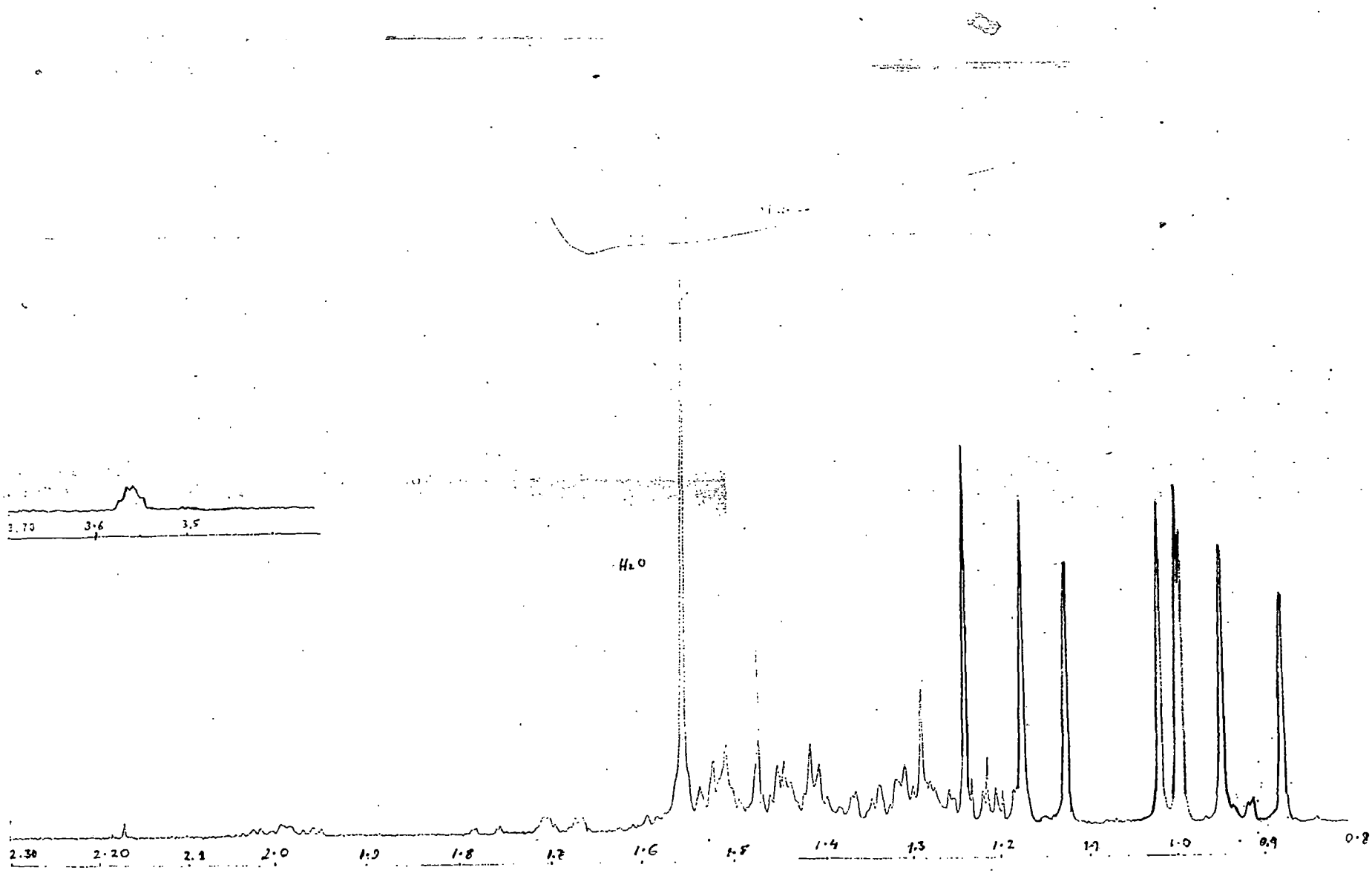


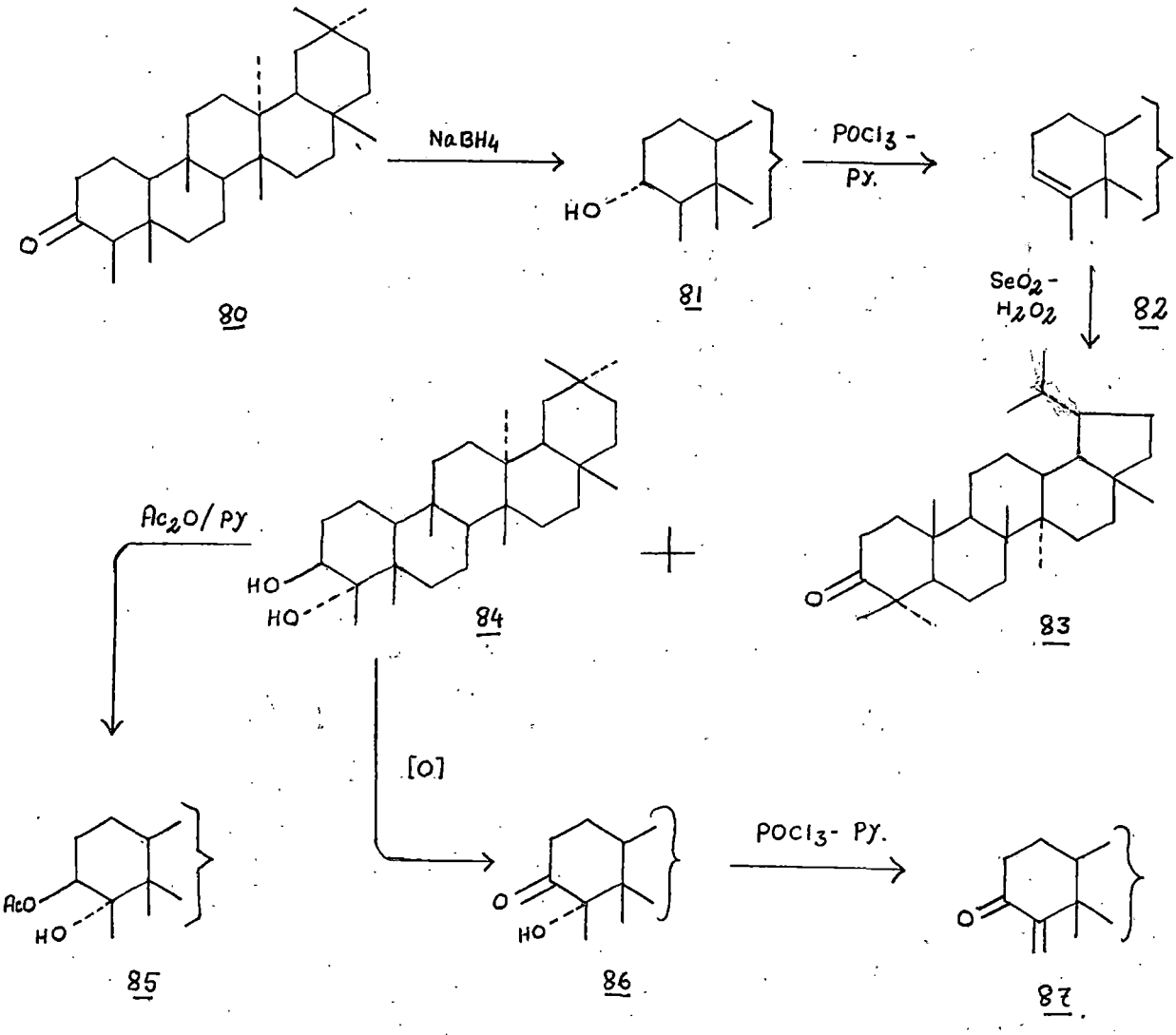
fig. 13 : ^{1}H NMR spectrum of friedelan 3β,4α-diol, 84.

each and one 6H) beteen (δ in ppm.) 0.8 to 1.17 ; one doublet of doublet (J= 3 and 8 Hz.) centred at 2.105 is probably due to methine proton at C-18; The two multiplets centred at 2.23 and 2.96 are accounted for axial and equatorial protons at C-2. Thus,compound E is proposed to be friedelan 3-oxo,4α-ol **86**.

The compound E was dehydrated with phosphorus oxychloride in pyridine when it afforded compound G, **87** *M.P.*208-9^{o}C. It gave UV (methanol) absorption at (λ_{max}) 220 nm. (fig.17) showing the presence of α,β unsaturated ketone. Further, IR spectrum showed peaks at 1690,1650 cm^{-1} confirming the presence of conjugated ketone moiety.

Hence, compound G was identified as friedelan-3-oxo,4(24)-ene, **87**.

The conversion of friedlin **80** to friedelan-3-oxo,4(24)-ene **87** is depicted in the following scheme:-

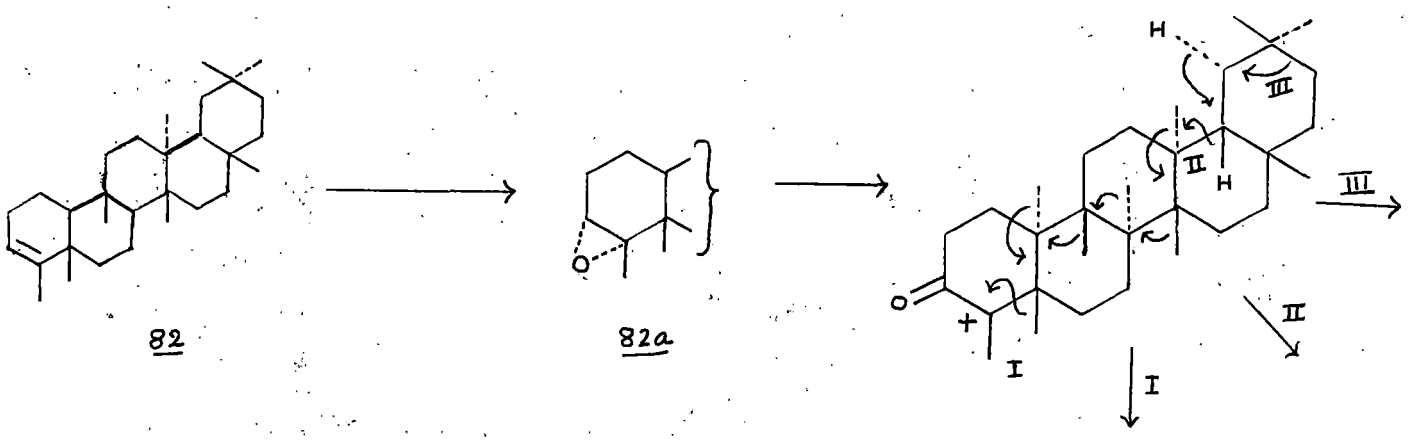


The mechanism suggested for lupanone formation is shown below :-

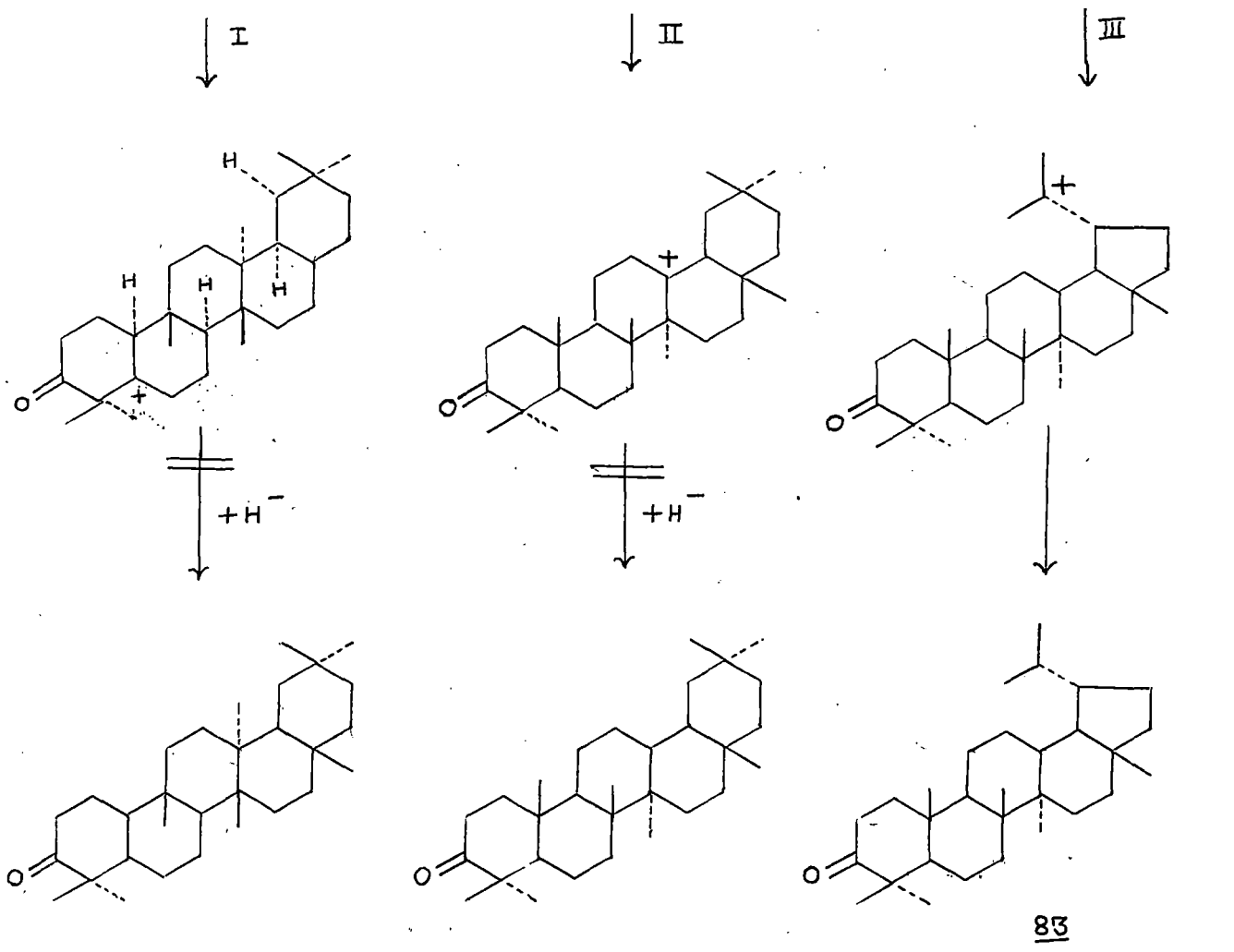
It is well known that unsymmetrical epoxide on treatment with Lewis acids like boron triflouride-ethearate causes epoxide ring opening with the formation of carbocation at the more substituted carbon atom to furnish a ketone by hydride transfer rearrangement[38].

In the present case the epoxide formed by the reaction with hydrogen peroxide at C_3-C_4 position of friedelene (82) probably undergoes this sort of ring opening to give a carbocation at C-4 position. Than there may undergo a backbone rearrangement which may involve 1,2 shifts of methyl groups and hydrogen atoms leading to the shift of the carbocation from C-4 to C-20 carbon. Since a hydride ion is produced during the formation of a ketone, this hydride ion attacks the C-20 carbocation to give lupanone (83).

It is reported [34,39] that friedel-3(4)-ene (and 3-hydroxy friedelane after dehydration) undergoes isomerisation of double bond in acidic medium to give glut-5(6)-ene /glut-5(10)-ene or β-amyrin / δ-amyrin which involve 1,2 shift(s) accompanied by loss of a proton whereas in the present case the epoxide ring rearrangement causing formation of hydride ion and a ketone, favours addition of this hydride ion but the addition of this hydride ion to the carbocation at C-5 or C-13 is not favoured energetically. Hence, further isomerisation of the carbocation at the extreme position is probably most favoured energet--ically to form the carbocation at C-20. The probable steps are represented in the following scheme :

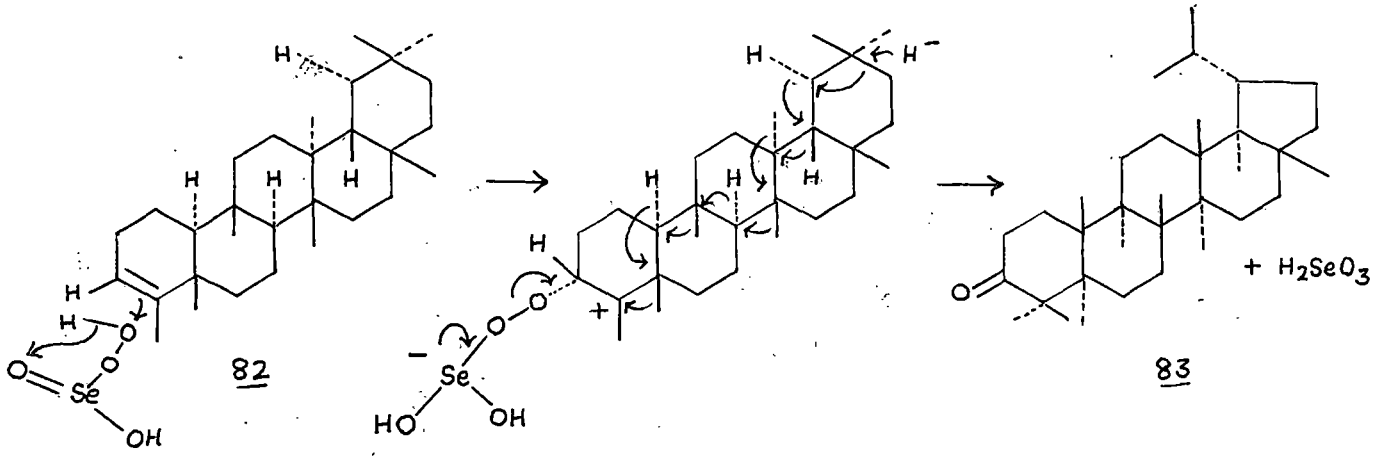


82 82a



83

The other possibility may involve the attack of olefinic double bond of friedel-3(4)-ene (82) by the peroxyselenic acid at C-3 position generating a peroxy organo selenious di-ion. This di-ion forms the ketone by the loss of a hydride ion and the carbocation at C-4 undergoes a series of 1,2 shifts leading to the formation of carbocation at C-20. The C-20 carbocation than accepts the hydride ion giving lupanone (83).



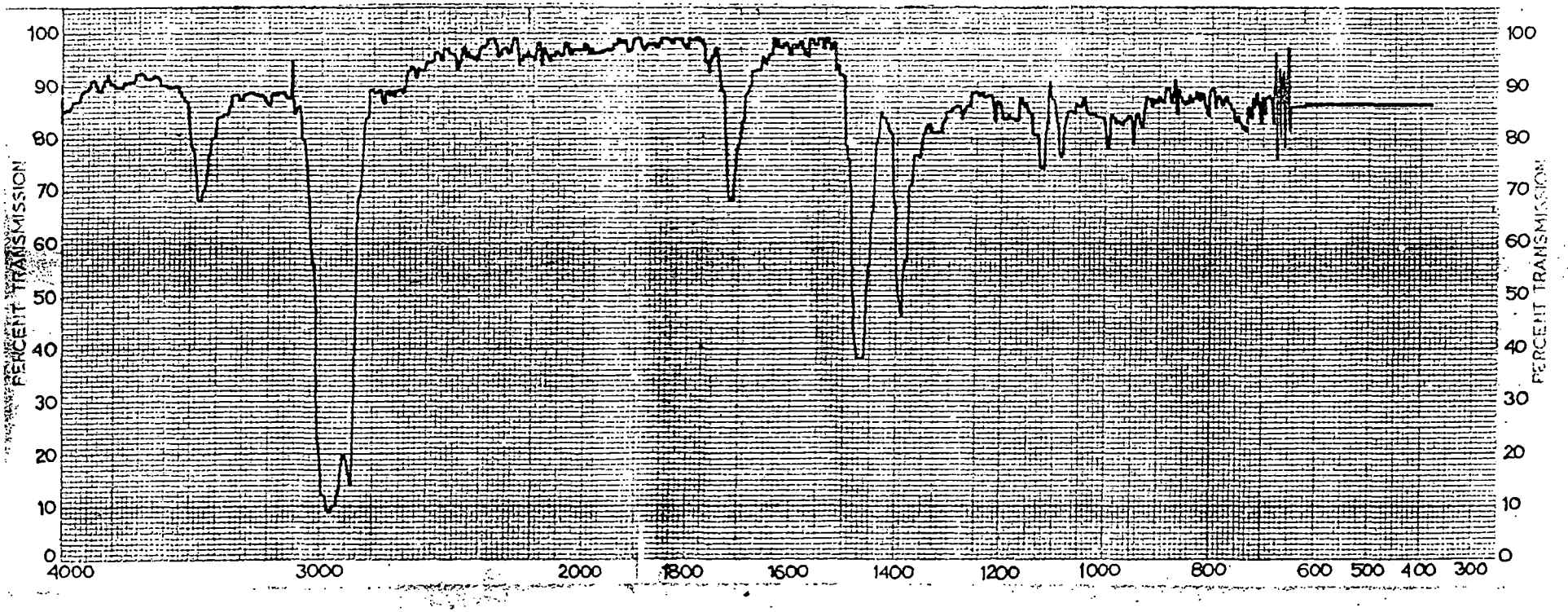


fig. 14 : IR spectrum of friedelan 3-oxo,4α-ol, 86.

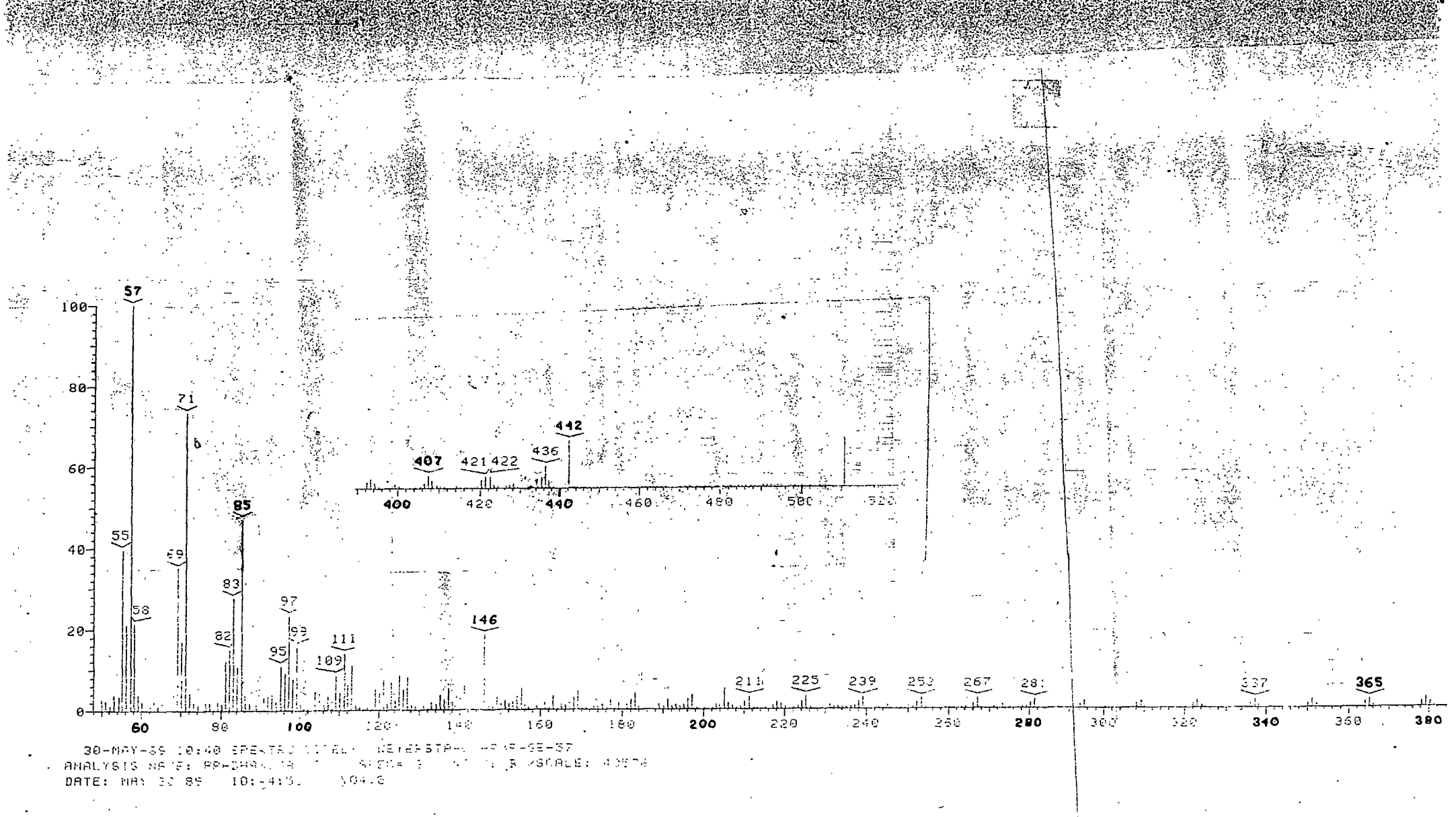


fig. 15 : Mass spectrum of friedelan 3-oxo,4α-ol, 86.

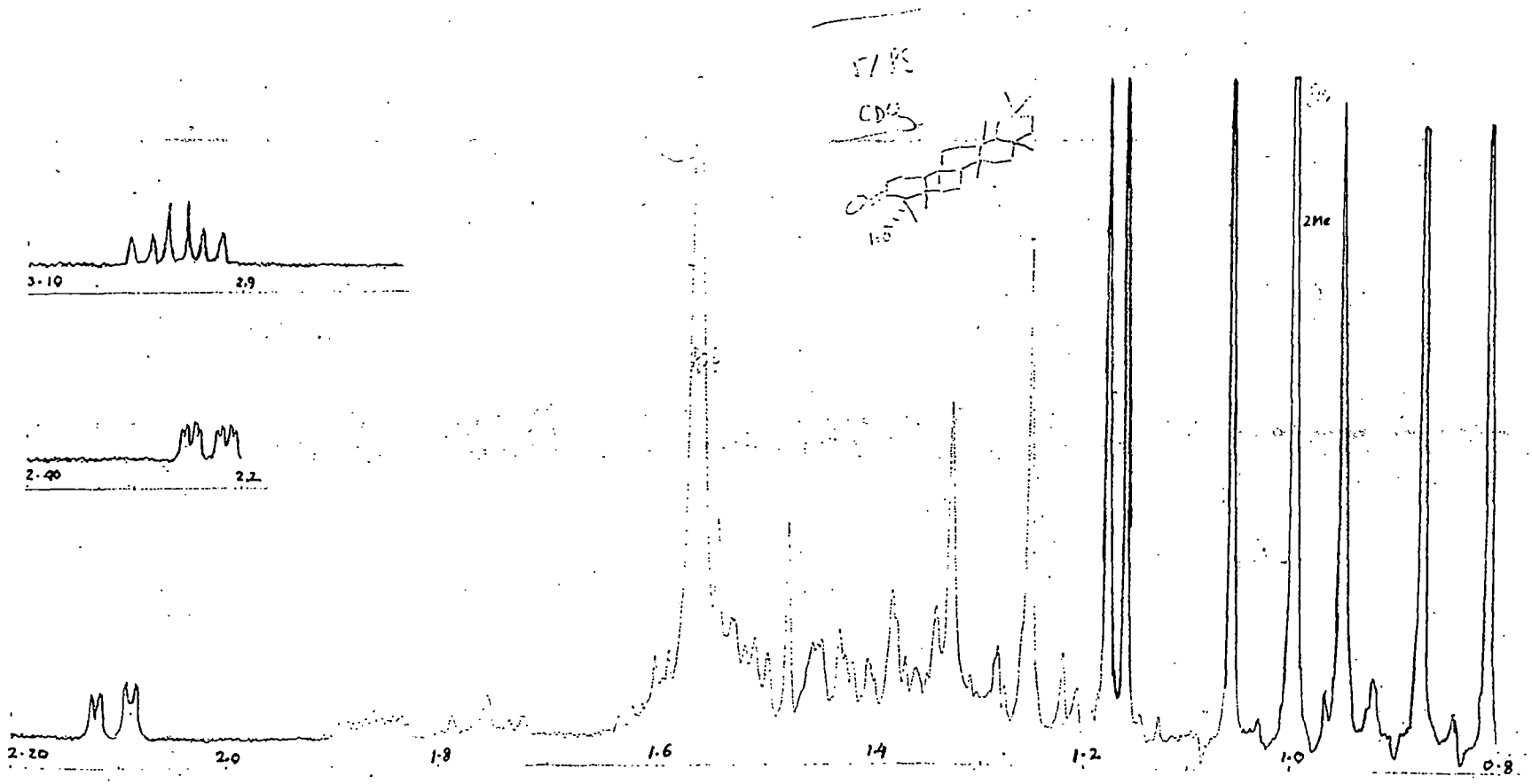


fig. 16 : ^{1}H NMR spectrum of friedelan 3-oxo,4α-ol, 86.

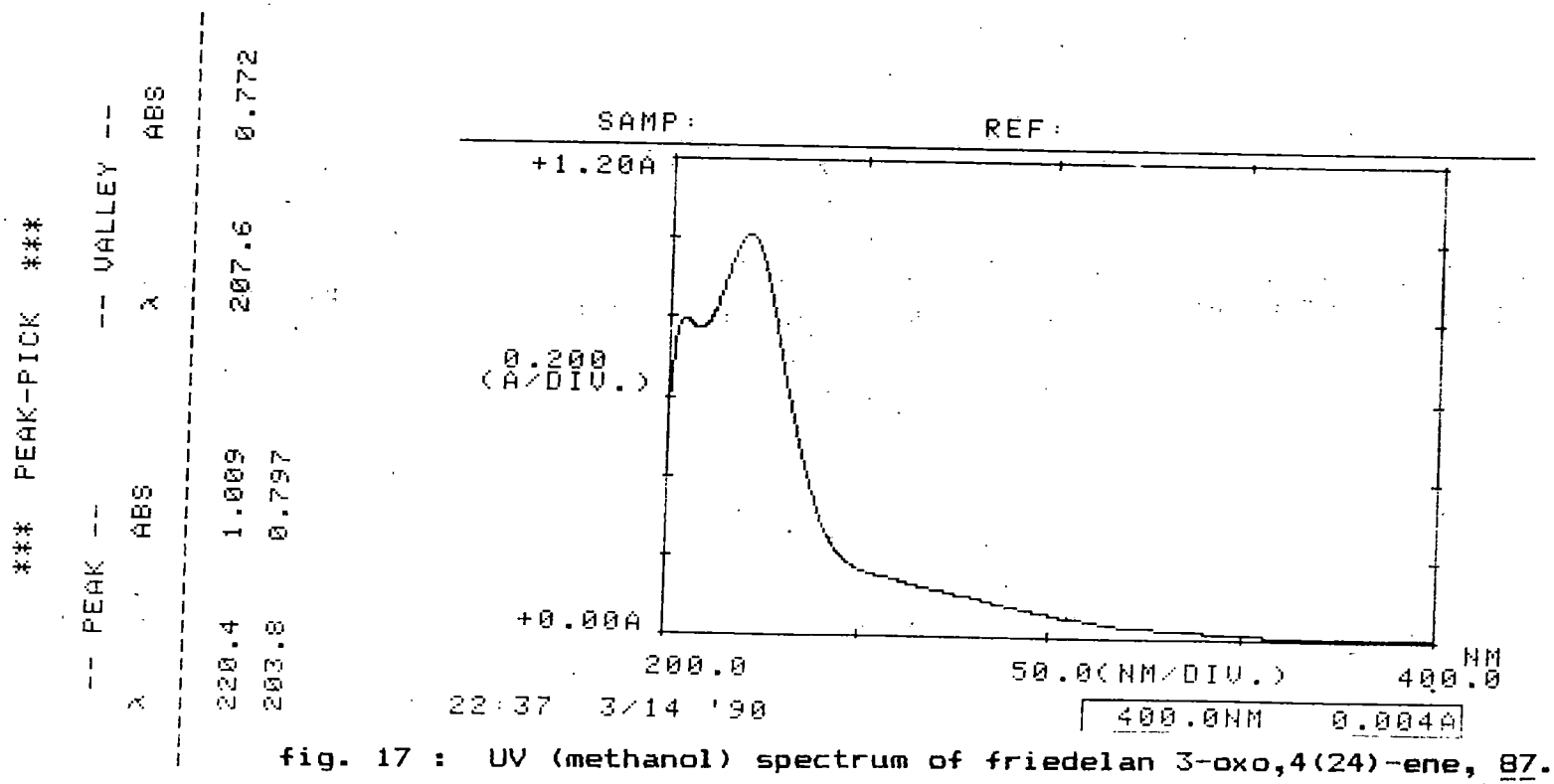


fig. 17 : UV (methanol) spectrum of friedelan 3-oxo,4(24)-ene, 87.

OXIDATION OF 3,4 DEHYDRO FRIEDELAN-27→15α OLIDE WITH SELENIUM DIOXIDE IN TERTIARY BUTANOL CONTAINING HYDROGEN PEROXIDE.

The compound 3,4-dehydro-friedelan 27 → 15α olide **91**, prepared from friedelan-3-oxo, 27→15α olide **88** (see experimental) was dissolved in tertiary butanol and refluxed with selenium dioxide in presence of hydrogen peroxide. After usual workup, the crude product was subjected to column chromatography and a single compound H was obtained on elution with benzene-chloroform (1:1).

Characterisation of compound H : Isolation of friedelan-3β,4α diol, 27→15-olide 92:

The compound H was crystallised from chloroform-methanol to furnish needle shaped crystals, *M.P.* 270-71°C; Its IR spectrum (fig. **18**) showed peaks at 3500 and 3440 cm^{-1} indicating the presence of two hydroxy groups and at 1760 cm^{-1} for carbonyl group of γ-lactone moiety. The mass spectrum (fig.**19**) indicated the molecular ion peak m/e at 472 (M,22%); other important peaks appeared at m/e 436 (M $-2H_2O$ 28)$^+$, 386 (33), 385 (100), 133 (66). Elemental analysis and mass spectral data showed the molecular formula to be $C_{30}H_{48}O_4$.

^1H NMR spectrum (fig.**20**) signals for different protons are recorded in tabular form as shown in table-V.

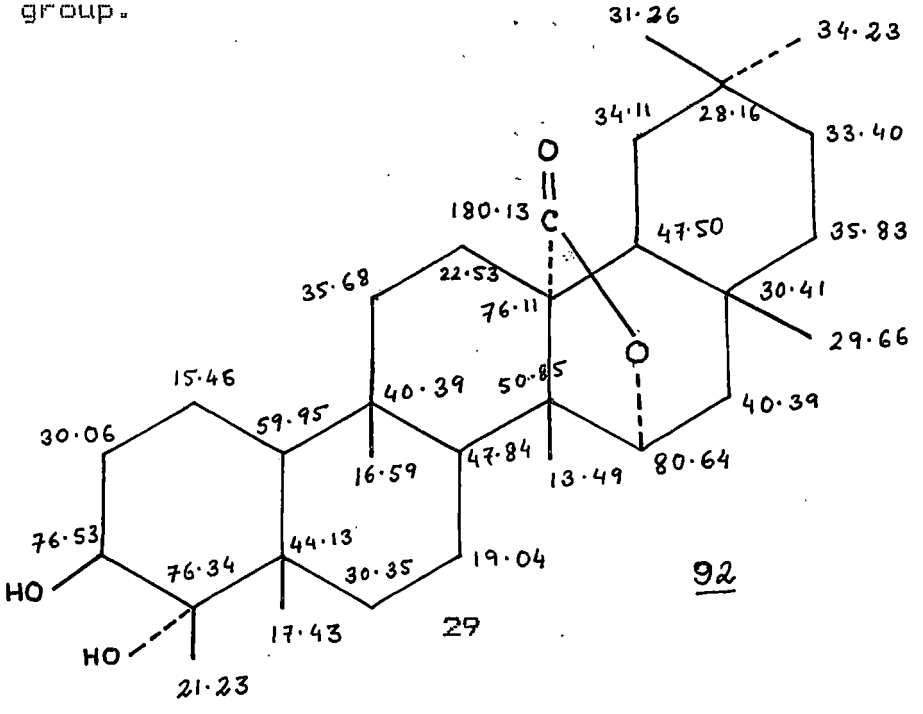
TABLE-V.

Chemical shifts. (δ in ppm.)	No.of protons.	Multiplicity of signals.	Probable assignment.
0.86	3	singlet	seven
0.94	3	"	tertiary
0.96	3	"	methyls.
0.99	3	"	
1.02	3	"	
1.05	3	"	

1.21	3	"	
2.02	1	triplet of doublet. (J = 3 & 13.5 Hz.)	methine proton (18α-H)
3.54	1	triplet. (J = 3 Hz.)	3α-H geminal to 3β-OH.
4.34	1	triplet. (J = 3 Hz.)	A methine proton geminal to lactonic O-atom.

The ^{1}H NMR signals of compound H was compared with friedelan 3β,4α diol 84 as discussed in Section C. The position and coupling values of the two protons attached to the C-2 and C-3 carbons are exactly similar and have the stereochemistry which is shown to be 3β,4α for the hydroxyl groups in compound H also.

The ^{13}C NMR spectrum (fig.21) accounted for 30-carbon atoms. APT experiment showed the existance of 7 $-CH_3$ as quartets, 10 $-CH_2-$ as triplets, 5 -CH- as doublets and 8 -C- as singlets. Among them the doublets that appeared downfield at 76.34 and 80.64 ppm. are due to carbon atoms bearing -OH group at C-3 and lactonic O-atom at C-15 respectively. The two downfield singlets at 180.13 and 76.11 ppm. are accounted for carbonyl carbon of the lactone moiety and C-4 bearing another -OH group.

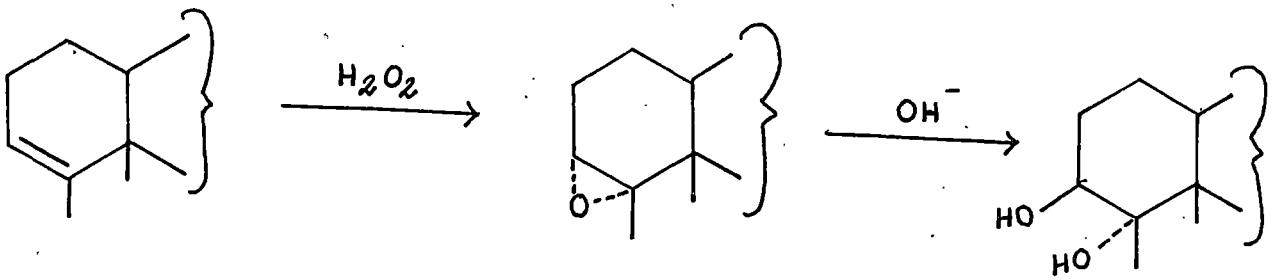


92

Thus from, ^{1}H NMR, Mass and ^{13}C NMR spectral studies the structure of compound H is proposed to be friedelan-3β,4α-diol 27→15α olide 92.

Mechanism proposed for the reaction :-

The formation of friedelan-3β,4α-diol 84 and friedelan-3β,4α-diol 27->15α olide 92 from 3(4)-dehydro-friedelan 82 and 3(4)-dehydro-odolactone 91 on oxidation with selenium dioxide containing hydrogen peroxide indicated that 3,4-epoxide is first formed with hydrogen peroxide. The epoxide is definitely formed at the less hindered alpha side to furnish 3α,4α-epoxide compound 91a which then undergoes epoxide ring cleavage by the attack of perhydroxy selenic acid from the β-phase to generate the trans diol D and H respectively.



82 or 91 — a — 84 or 92

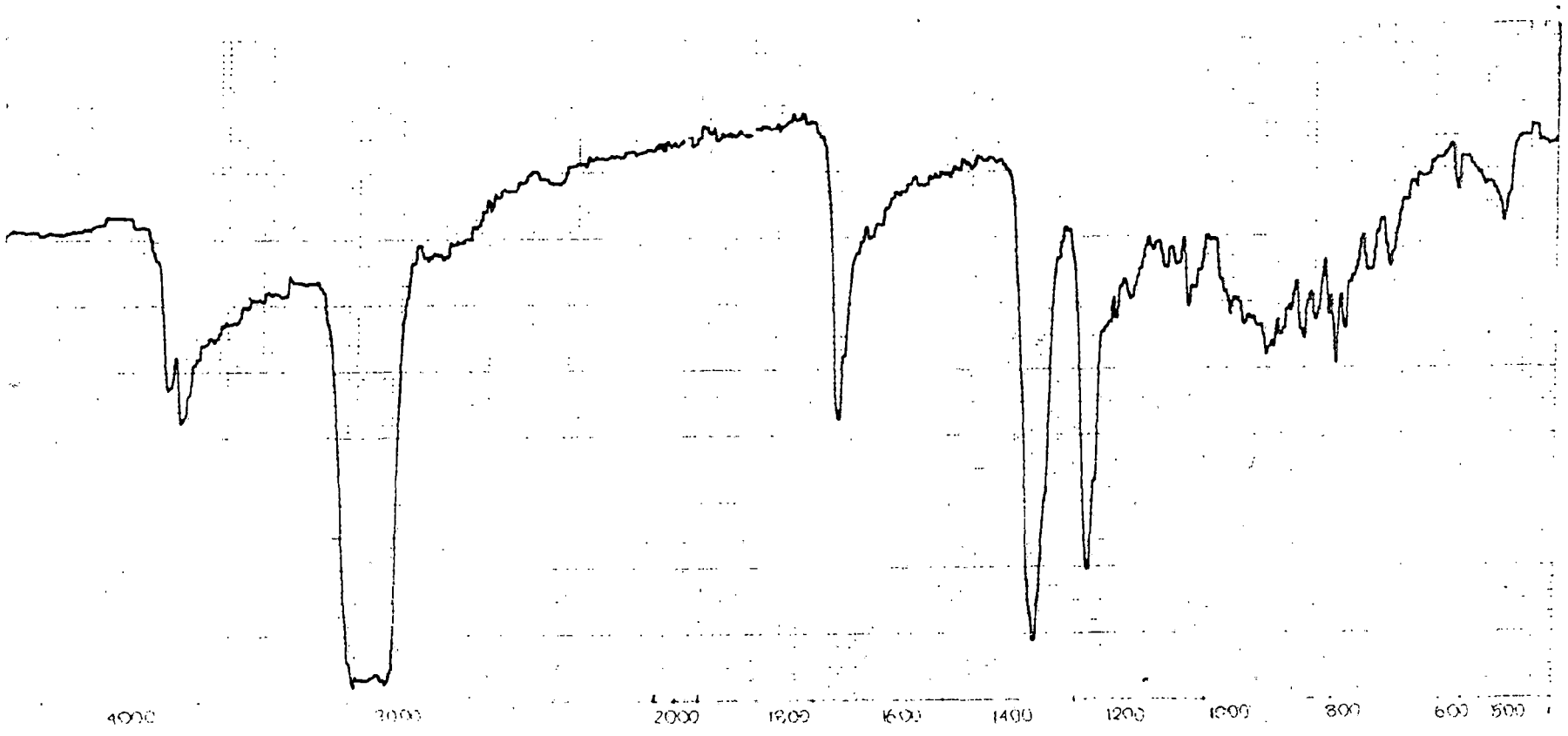


fig. 18 : IR spectrum of friedelan 27→ 15α-olide,3β,4α-diol, 92.

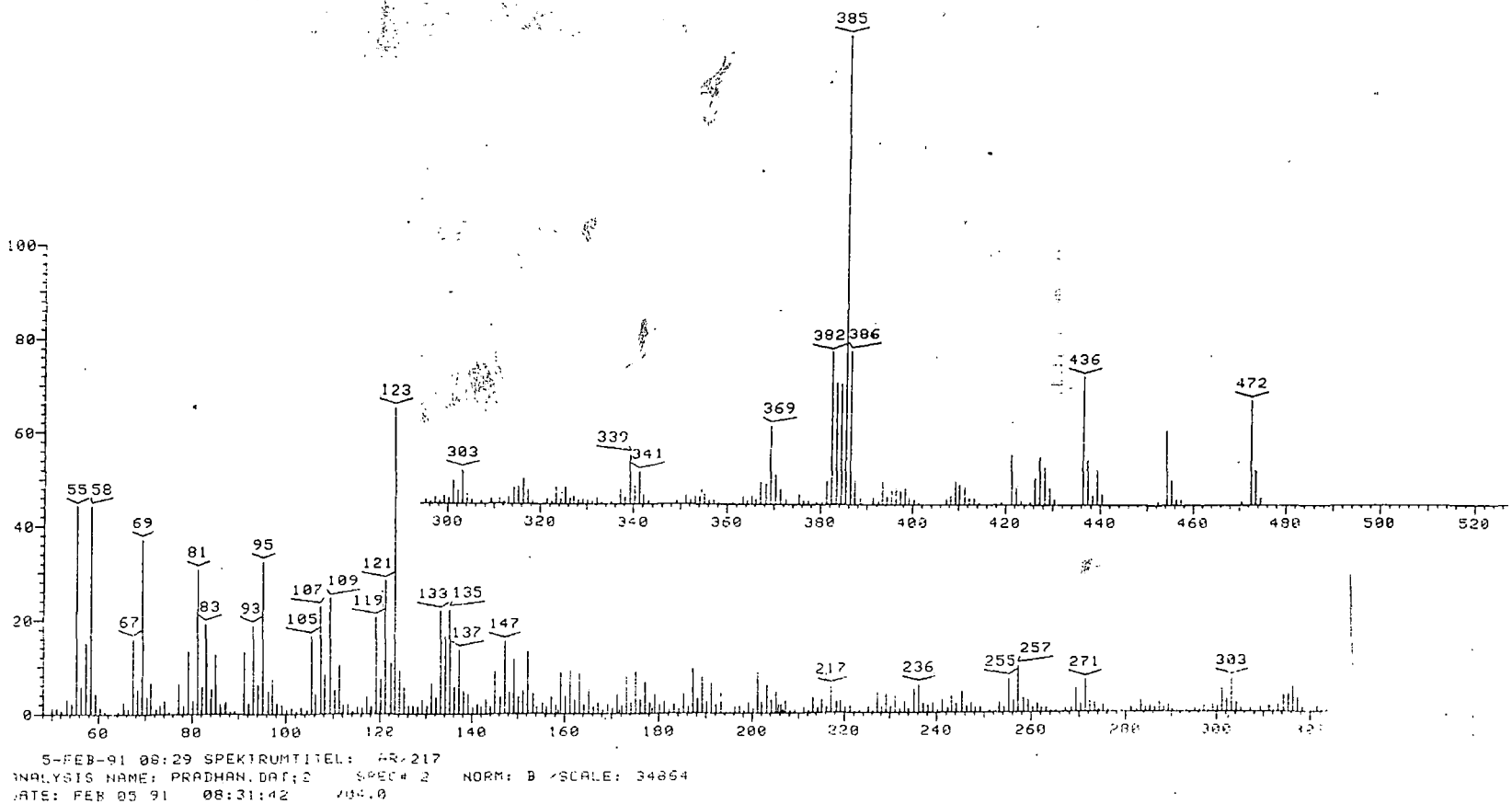


fig. 19 : Mass spectrum of friedelan 27→15α-olide,3β,4α-diol, 92.

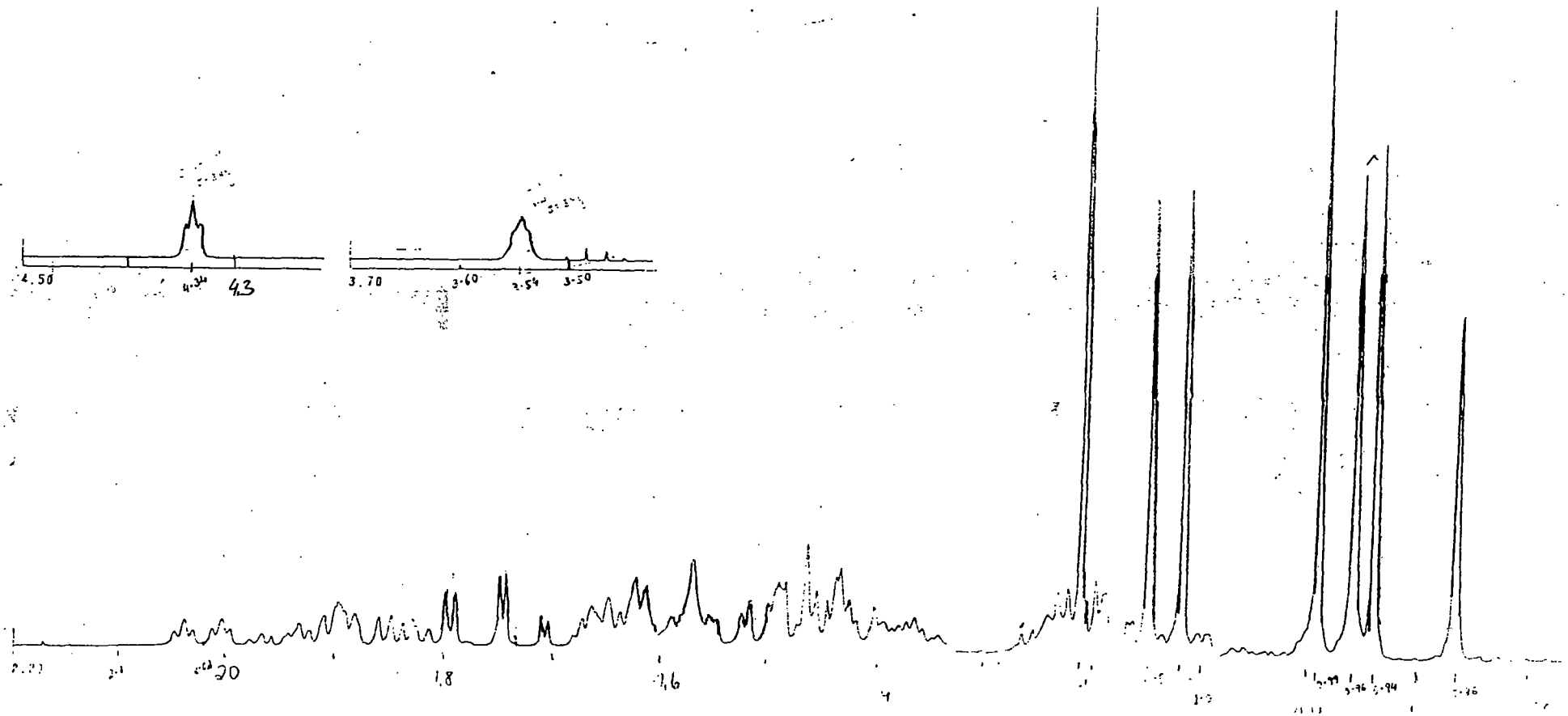


fig. 20 : ^{1}H NMR spectrum of friedelan 27→15α-olide,3β,4α-diol, 92.

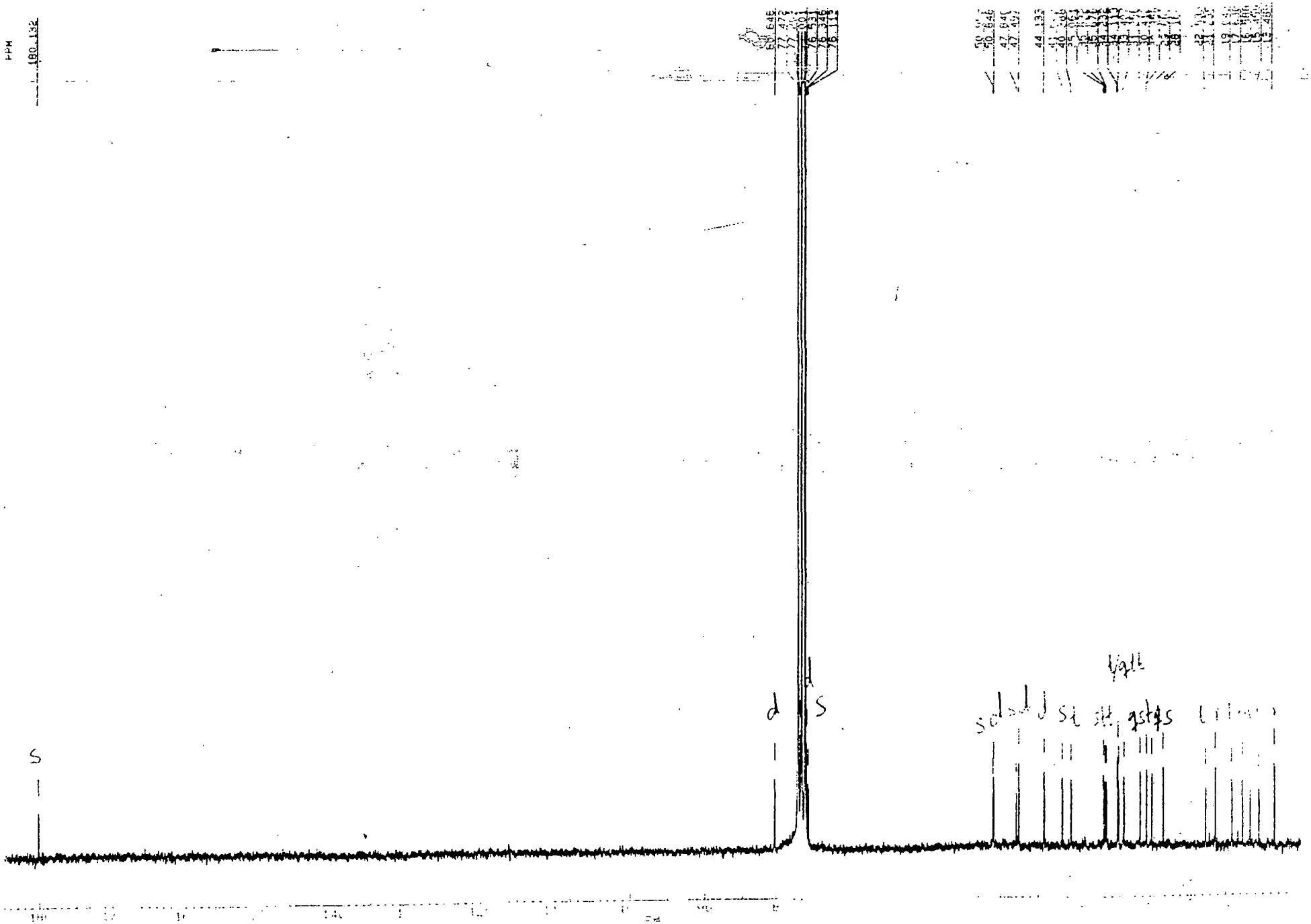


fig. 21 : ^{13}C NMR spectrum of friedelan 27→15α-olide,3β,4α-diol, 92.

Melting points are uncorrected. The petroleum ether used throughout the investigation had *B.P.* of 60-80°c. The *INFRA RED* spectra were recorded in *BECKMAN* IR-20 spectrophotometer. The UV absorption spectra were taken in *BECKMAN* DU-2 spectrophotometer. Mass spectra were determined with an MS-9 mass spectrometer. ^1H NMR spectra were recorded with *VARIAN* A-60 or HA-100 spectrometer using deuterated chloroform solution containing tetra methyl silane as reference. Silica gel used for column chromatography was of 60-120 mesh (B.D.H. and glaxo). TLC was done on chromatoplates prepared on glass strips with silica gel using benzene-petrol mixture as solvents and the spots were developed in an iodine chamber.

ISOLATION OF LUPEOL **69** *FROM XANTHOXYLUM BUDRUNGA.*

About five kilogram of air dried finely powdered bark of *Xanthoxylum budrunga*[32] was extracted with benzene in a soxlet extractor for 48 hours. The extract was cooled and the solvent was distilled off. The residual gummy mass was then dissolved in minimum volume of benzene, chromatographed over silica gel column and elution with petrol -benzene (4:1) mixture furnished lupeol **69** (10 gm.). Lupeol was further purified by repeated crystallisation from chloroform-methanol mixture, *M.P.* 215-6°C, $[\alpha]_D = -33^\circ$, found to be identical with authentic sample of lupeol (Co-tlc, *M.M.P.* and Co-IR).

HYDROGENATION OF LUPEOL TO LUPANOL **70**.

5.0 gm. of lupeol was dissolved in 250 ml of distilled ethyl acetate and 1.6 gm. of palladised charcoal (E.Merck) was added. Then it was reduced with hydrogen at atmospheric pressure. The catalyst was then filtered off, the solvent was distilled out and the residue on crystallisation from chloroform-methanol mixture gave fine crystals of lupanol (4.5 gm.), *M.P.* 207-8°c, $[\alpha]_D = +17.8^\circ$, identical with authentic lupanol (Co-IR, M.M.P.).

DEHYDRATION OF LUPANOL TO 2,3-DEHYDRO LUPANE 71.

2.5 gm. of lupanol was dissolved in 10 ml of distilled pyridine (Py) and 5 ml of distilled phosphorus oxychloride ($POCl_3$) was added. The mixture was then heated over water bath for 4 hours. It was then cooled, diluted with water cautiously to destroy excess $POCl_3$ and extracted with ether. Then it was repeatedly washed with water till neutral, dried with anhydrous sodium sulphate (Na_2SO_4) and finally the ether was distilled off giving a yellowish white gummy mass.

The gummy substance was then dissolved in minimum volume of benzene and chromatographed over silica gel (100 gms.) column developed with petroleum ether and eluted with solvents as shown in the table below –

TABLE-I

Eluent.	Fraction of 50 ml each.	Residue on distillation.	M.P.
petrol	1-5	oil	
petrol-benzene (4:1)	6-12	solid 1.4 gms.	181-2°c

Further elution with more polar solvents did not afford any solid material.

Fractions 6-12 were combined together. This on crystallisation with $CHCl_3$-MeOH afforded needle shaped crystals of lup-Δ^2-ene **71**. *M.P.* 186-7°C, $[\alpha]_D$ = + 13.4°, ν_{max} 730 and 1640 cm^{-1}, produced yellow colour with tetra nitro methane (TNM).

OXIDATION OF LUP-Δ^2-ENE 71 WITH SELENIUM DIOXIDE IN TERTIARY BUTANOL CONTAINING HYDROGEN PEROXIDE.

A solution of lup Δ^2-ene (1.0 g) dissolved in tertiary butanol (t-BuOH) 150 ml. containing selenium dioxide (SeO_2) 0.8 g and hydrogen peroxide (H_2O_2) 2 ml. (30%) was refluxed over water bath. After 40 hours, black selenium metal separated out indicating the

completion of the reaction. It was cooled and poured in ice cold water when a white solid appeared which was extracted with ether and the ether layer was washed with 5% Na_2CO_3 solution three times followed by water repeatedly till neutral. The ether layer was then dried over anhy. Na_2SO_4 and the filtered solution on evapouration to dryness yielded a gummy residue (0.5 g).

The alkali-wash was kept aside for further treatment.

ISOLATION OF LUPAN 2,3 DIOL **72**.

The neutral gummy mass (0.5 g) was dissolved in minimum volume of benzene and chromatographed over silica gel (40 g). The chromatograph was developed with petrol and eluted with solvents as in table-

TABLE-II

Eluent	Fractions of 50 ml. each.	Residue on distillation.
1. petrol	1-4	oil.
2. petrol-benzene (3:2)	5-10	oil.
3. petrol-benzene (1:4)	11-15	oil.
4. benzene-chloroform (4:1)	16-20.	solid.

Further elution with more polar solvents did not furnish any more solid material.

The fraction (16-20) were combined and crystallised from $CHCl_3$-MeOH, *M.P.*245-46^{o}C; its IR spectrum showed a broad peak at 3540 cm^{-1}. indicating the presence of hydroxy group and hence it was acetylated.

ACETYLATION OF FRACTION (16-20) *TO LUPAN 2β,3α DIYL ACETATE* **73**.

The compound **72**.(0.4 g) was dissolved in 4 ml.pyridine (Py.) and 4 ml. of acetic anhydride (Ac_2O) was added. The mixture was than kept over

water bath for 4 hours and then poured in ice cold water when a white solid separated out. It was filtered through suction, washed with water and dried. The dried mass was then chromatographed over silica gel column with the following solvents as shown in the table below:-

TABLE-III.

Eluent.	Fraction of 50 ml. each.	Residue on distillation.
1. petrol	1-3	nil.
2. petrol-benzene (4:1)	4-6	nil.
3. petrol-benzene (3:2)	7-10	white solid. (0.35 g)

Further elution did not afford any more solid.

The fractions 7-10 were collected together and crystallised from $CHCl_3$-MeOH mixture giving colourless crystals, *M.P.* 220-21°C, $[\alpha]_D$= +23.4°, identified as lupan 2β,3α diyl acetate 73.

ANALYSIS REPORT

Found :	C 77.13 ;	H 10.01.
Calculated for $C_{34}H_{56}O_4$:	C 77.27 ;	H 10.61.

IR (Nujol): ν_{max} 1750, 1270 and 1250 cm^{-1}. (2x CH_3-CO-O-) fig.1.

MS : m/e 528 (M^+, 86), 513 (30), 488 (43), 468 (78), 408 (100), 393 (88), 365 (52.5), 231 191 (86), 187 (98), 123 (94) fig.2.

^1H NMR ($CDCL_3$): (δ in ppm.) 0.77 and 0.84 (dd,6H,CH_3-CH-CH_3)

0.76,0.91,0.95,0.98,1.03 and
1.07 (6s,18H, 6x t-CH_3).
2.01 and 2.07 (2s,6H,2x -$OCOCH_3$)
4.96 (dd,3H, AcO-CH-CH_2-)
5.07 (d, 2H, AcO-CH-CH-OAc)
fig.3.

TREATMENT OF THE ALKALI WASH.

The alkali wash that remained after separation of neutral part was treated with 20% HCl till whole solution was slightly acidic.Since no solid material separated out, the solution was rejected.

ISOLATION OF BETULINIC ACID FROM BISCHOFIA JAVANICA.

Five Kg. of air dried finely powdered bark of *Bischofia Javanica*[33] was extracted with benzene in a soxlet extractor and distillation of the solvent gave a gummy residue, which was taken up in ether. Then the ether solution was treated with aqueous alkali (20% NaOH) and the alkali layer was separated from ether layer.(The ether layer containing neutral compounds was rejected.) The alkali layer on acidification with dil HCl yielded solid betulinic acid **74.** which was filtered through suction, washed repeatedly with water till neutral and dried properly for further work.

ESTERIFICATION OF BETULINIC ACID **74.**

About 5 gm. of betulinic acid was dissolved in ether and alkaline ethereal solution of N-nitroso N-methyl urea (8.0 gm.) was added. The ether solution was kept for one night in a freeze. It was acidified with few ml.of acetic acid to destroy excess diazomethane, washed with water till neutral and the solvent was evapourated to give crude methyl ester of betulinic acid. The crude ester was dissolved in minimum volume of benzene and chromatographed over silica gel column with eluents as shown in tabular form.

TABLE-IV.

	Eluent.	Fraction on 50 ml. each.	Residue on distillation.
1.	Petrol	1-3	nil
2.	Petrol-benzene. (4:1)	4-7	nil
3.	Petrol-benzene (3:2)	8-15	white solid. (0.4 g)

Further elution with more polar solvents did not afford any solid. The fractions 8-15 were combined and crystallised from $CHCl_3$-MeOH, *M.P.* 223-4°C, $[\alpha]_D$= +5°; IR: 3520 (-OH), 1735,1260 ($-COOCH_3$), 1660,870 cm^{-1}. ($=CH_2$), which were identical with authentic sample of methyl betulinate **75**.(Co. tlc, & *M.M.P.*).

HYDROGENATION OF METHYL BETULINATE **75**.

3.0 g of methyl betulinate dissolved in distilled ethyl acetate was reduced with hydrogen gas in presence of palladised charcoal catalyst at atmospheric pressure. The catalyst was filtered off,solvent was removed and the residue obtained was crystallised from $CHCl_3$-MeOH to give fine crystals of methyl dihydro betulinate **76**. *M.P.* 236-7°C, IR : 3500 (-OH), 1735, 1250 ($-COOCH_3$)cm^{-1}. identical with authentic sample (CO-tlc & *M.M.P.*).

DEHYDRATION OF METHYL DIHYDRO BETULINATE **76**.

3.0 g of methyl dihydro betulinate was dehydrated with dry Pyridine (8 ml.)and distilled $POCl_3$ (4 ml.). After usual work up, the gummy residue was chromatographed over silica gel. On elution with petrol-benzene (4:1) a solid was obtained, which was crystallised from $CHCl_3$-MeOH yielding white crystals of 2,3 dehydro methyl dihydro betulinate **77**.*M.P.* 228-9°C,IR :1730,1260 ($-COOCH_3$),1640,850 (-CH=CH-),gave yellow colour with TNM, identical with authentic sample (Co-tlc & m.m.p.)

OXIDATION OF 2,3 DEHYDRO METHYL DIHYDRO BETULINATE **77** *WITH* SeO_2 *IN TERTIARY BUTANOL CONTAINING* H_2O_2.

1.0 g of the compound was dissolved in 150 ml. of t-BuOH and refluxed with a mixture of SeO_2 (0.8 g) and H_2O_2 (30%, 2 ml.) for 40 hours. After usual workup, the gummy residue obtained from the neutral ether layer was chromatographed over silica gel column. On elution with solvents of increasing polarity, a mixture of benzene-$CHCl_3$ (1:1) gave a gummy solid difficult to crystallise. The IR spectrum of the crude product indicated the presence of hydroxy function and hence it was acetylated with Ac_2O-Py. mixture.

The alkali layer was acidified with 20% HCl till slightly acidic and since no solid material separated out, it was rejected.

ACETYLATION OF THE GUMMY SOLID : ISOLATION OF 2β,3α-*DIACETOXY METHYL DIHYDRO BETULINATE* **79**.

The gummy solid (0.6 g) was acetylated with Py. (10 ml.) and Ac_2O (10 ml.). The solid material obtained on usual workup was chromatographed over silica gel column and on elution with benzene-petrol (4:1) mixture yielded a white solid. It was crystallised from $CHCl_3$-MeOH to afford white crystals identified as 2β,3α-diacetoxy methyl dihydro betulinate **79**. *M.P.* 209-10°C from spectral studies.

ANALYSIS REPORT.

Found :	C 72.8 ;	H 9.10.
Calculated for $C_{35}H_{56}O_6$:	C 73.4 ;	H 9.79.

IR : (Nujol) ν_{max} 1730, 1230 cm^{-1}. ($-CO-CH_3$).
1720, 1220 cm^{-1}. ($-CO-O-CH_3$).
fig.4.

Mass : m/e 572 (M^+), 513, 512, 470, 452, 437, 411, 393, 377, 203, 191, 187 (100%).
fig.5.

^{1}H NMR ($CDCl_3$):	0.74 & 0.85 (dd,6H,CH_3-CH-CH_3)
(δ in ppm.)	0.90, 0.95, 0.96, & 1.05 (4s,15H,5X t-CH_3)
	2.01 & 2.06 (2s,6H,2X-O-CO-CH_3)
	3.64 (s,3H,-CO-O-CH_3)
	4.76 (dd,-CH_2-CH-OAc)
	5.06 (d, AcO-CH-CH-OAc)

fig.6.

ISOLATION OF FRIEDELIN FROM THE BARK OF QUERCUS SUBER, CORK.

5 kg. of finely powdered dry cork, the bark of *Quercus suber*[34], was extracted with benzene in a soxlet extractor for 48 hours. After removal of the solvent, a white solid separated out. The solid was dissolved in minimum volume of benzene and chromatographed over silica gel. Elution of the column with petrol-benzene (4:1) mixture gave friedlin, which was crystallised from chlorform-methanol to give crystals of friedlin **80**, *M.P.*262-3^{o}C, $[\alpha]_D$= -48.7^{o}, IR : 1715 cm^{-1}.for saturated ketone.

REDUCTION OF FRIEDELIN WITH SODIUM BOROHYDRIDE IN DIOXANE

3.0 g of friedlin was dissolved in 200 ml. of dioxane and 150 ml. of methanol was added. Then 4.0 g of $NaBH_4$ was added to the mixture and it was kept at room temperature for 12 hours. The mixture was than diluted with water and acidified with dil HCl (1:4) till slightly acidic. The solid separated out was filtered with suction, washed with water till neutral and dried. It was then crystallised from $CHCl_3$-MeOH giving needle shaped crystals of friedelan 3β-ol **81**, *M.P.*268-9^{o}C, IR : 3540 cm^{-1}.(-OH), identified by comparison with authentic sample (Co-tlc,& *M.M.P.*).

*DEHYDRATION OF FRIEDELIN 3β-ol **81** BY PHOSPHORUS OXYCHLORIDE-PYRIDINE MIXTURE.*

2.5 g of friedelan 3β-ol was dissolved in 10 ml. of pyridine and

5 ml. of phosphorus oxychloride was added. The mixture was than heated in water bath for 4 hours. After usual workup, the gummy mass obtained was chromatographed. On elution with petrol, a white solid material (1.3 g) was obtained, which was repeatedly crystallised from petrol-$CHCl_3$ to furnish white crystals of 3(4)-dehydro friedlin **82**, *M.P.*263^{o}C IR :1650 and 800 cm^{-1}. gave yellow colour with TNM.

Found :	C	87.60%	;	H 12.01%
Calculated for $C_{30}H_{50}$:	C	87.73%	;	H 12.26%

OXIDATION OF 3(4)-DEHYDRO FRIEDELIN **82** *WITH SELENIUM DIOXIDE IN TERTIARY BUTANOL CONTAINING HYDROGEN PEROXIDE.*

A solution of friedel Δ^{3}-ene (1.0 g) dissolved in t-butanol (150 ml.) containing selenium dioxide (0.8 g) and hydrogen peroxide (30%, 2 ml.) was refluxed for 40 hours. After workup, the residual gummy mass obtained from the neutral part was chromatographed. The column was eluted with solvents as shown in table-V.

The alkali wash on acidification did not afford any solid material and hence it was rejected.

TABLE-V.

Eluent.	Fraction 50 ml. each.	Residue on distillation.
1. petrol	1-8	oil
2.petrol-benzene (4:1)	9-12	solid, (0.15 g)
3. " " (3:2)	13-16	solid, (0.12 g)
4. " " (1:1)	17-20	nil
5. benzene-chloroform (4:1)	21-25	solid, (0.4 g)

Further elution did not afford any more compound.

Fractions 9-12 were collected together and crystallised from petrol-

$CHCl_3$, *M.P.* 263-4°C.,which were unreacted compound identified by comparison with authentic sample (m.m.p. & Co-tlc).

Fractions 13-16 on crystallisation from $CHCl_3$-MeOH afforded needle shaped crystals, *M.P.* 207-8°C, $[\alpha]_D$ +16°, IR : 1715 cm^{-1}. identified as lupanone **83**, from spectral analysis (^1H NMR & Mass) and comparison with authentic lupanone (*M.M.P.*,Co-tlc and Co-IR)

ANALYSIS REPORT.

Found : C 83.8 ; H 12.0%.

Calculated for $C_{30}H_{52}O$: C 84.12; H 12.14%.

IR (Nujol) : ν_{max} 1715 cm^{-1}.

fig.7

Mass : m/e 426 $(M)^+$, 411, 383, 355, 206 205, 163, 109, 107 (100)

fig.8

^1H NMR ($CDCl_3$): (δ in ppm.)

0.75 and 0.83 (dd,6H,CH_3-CH-CH_3)

0.75, 0.98, 0.93, 1.02 and 1.07 (5s,18H,6X $-CH_3$)

1.88 and 2.44 (2m,$-CH_2-CH_2-C=O$)

fig.9

Fractions 21-25 were combined and than crystallised from $CHCl_3$-MeOH, *M.P.* 235-6°C, $[\alpha]_D$=+ 14.1°,IR : 3340,3480 cm^{-1}.(-OH),identified as friedelan 3β,4α diol **84**, from ^1H NMR and Mass analysis.

ANALYSIS REPORT.

Found : C 80.21; H 11.10% ;

Calculated for $C_{30}H_{52}O_2$: C 81.08 ; H 11.71%

IR (Nujol) : ν_{max} 3340 and 3480 cm^{-1}.(-OH)

fig.11.

Mass : m/e 444 $(M)^+$, 429, 426, 411, 341, 273, 218,208 163 and 161.

fig.12

^{1}H NMR ($CDCl_3$): (δ in ppm.)	0.88,0.97,0.99,1.00,1.02,1.12 1.17 and 1.24 (8s,24H,8X-CH_3) 3.56 (AB_q, -CH-CH_2-, J = 3 & 7 Hz.)

fig.13

The compound **84** ,on acetylation with Ac_2O-Py mixture furnished the corresponding mono acetate **85**, *M.P.*245-6^{0}C, $[\alpha]_D$= +24^0, IR: 3500 (-OH) 1720,1280 cm^{-1}.(-$OCOCH_3$); Mass : 486 $(M)^+$; PMR : (δ) 0.9-1.3 (8s,24H, 8X t-CH_3),2.1 (s,3H,-$OCOCH_3$), 4.75 (t,1H, J = 3 Hz.)

OXIDATION OF FRIEDELIN 3β,4α DIOL **84** *BY JONES' REAGENT.*

0.2 g of friedelan 3β,4α diol **84** ,was dissolved in acetone (100 ml.) and Jones reagent was added dropwise with shaking untill a faint orange colour persisted.The mixture was kept at room temperature for 1 hour, diluted with water and extracted with ether. The ether layer was washed throughly with water, dried with anhydrous Na_2SO_4 and the ether on evapouration gave a residue,which was chromatographed. On elution with petrol-benzene (2:3) mixture, a solid mass was obtained which was crystallised from $CHCl_3$-MeOH to give white crystals, *M.P.* 252-3^{0}C; IR : 1715 (C=O) and 3470 cm^{-1}.(-OH), identified as friedelan 3-oxo 4α-ol from spectral analysis.

ANALYSIS REPORT.

IR (Nujol) : ν_{max}	3470 (-OH), 1715 cm^{-1}.(C=O)

fig.14

Mass : m/e	442 (M^+), 436, 407, 365, 281, 267, 239, 225, 211, 146, 85.

fig.15

^{1}H NMR ($CDCl_3$): (δ in ppm.)	0.80,0.87,0.95,1.00,1.05,1.16,1.17 (7s,3H each and one 6H,24H, 8-Me) 2.105 (dd, J= 3 Hz.and J= 8 Hz.) 2.23 and 2.96 (2m)

fig.16

DEHYDRATION OF FRIEDELAN 3-OXO 4α-OL **86** *BY* $POCl_3$-Py :

0.2 g of friedelan 3-oxo 4α-ol **86**,was dissolved in Py.(4 ml) and $POCl_3$ (1 ml)was added. The mixture was then heated over waterbath for 4 hours. After usual workup, the gummy mass was chromatographed and on elution with petrol, a solid mass was obtained which was crystallised from petrol, *M.P.* 208-9°C; UV : 220 nm. (fig. 17) for (CH_2=CH-C=O), IR :1690,1550 and 850 cm^{-1}.identified as friedelan 4(24)-ene 3-one **87**.

ISOLATION OF FRIEDELAN 3-OXO 27→15α OLIDE (ODOLACTONE) FROM THE BARK OF GYNOCARDIA ODORATA.

About 5 kg. of dry finely powdered bark of *Gynocardia odorata*[35], was extracted with benzene in a soxlet extractor for 48 hours. After the removal of solvent, the gummy mass was dissolved in minimum volume of benzene and chromatographed over silica gel. Elution of column with petrol-benzene (4:1) afforded a keto lactone, *Odolactone*[35] which was friedelan 3-oxo 27→15α olide,**88**. It was crystallised from $CHCl_3$-MeOH; *M.P.*>320°C, $[\alpha]_D$= -47.06°. Found : C 79.0% ; H 10.13% ,calculated for $C_{30}H_{46}O_3$: C 79.30% ; H 10.13%.

REDUCTION OF ODOLACTONE BY $NaBH_4$ *IN DIOXANE CONTAINING METHANOL.*

3.0 g of odolactone was reduced with $NaBH_4$ (6 g) in dioxane 200 ml.and methanol 150 ml. After usual workup, the reduced gummy product was dissolved in minimum volume of benzene and chromatographed. On elution with petrol-benzene (1:4) gave a solid material which was crystallised from $CHCl_3$-MeOH to give epi-odollactone (3β-hydroxy friedelan 27→15α olide) **89**. *M.P.*>320°,$[\alpha]_D$= -2.48°,

IR (Nujol) : ν_{max} 3520 (-OH) and 1740 cm^{-1} (γ-lactone)

Found :	C 78.90;	H 10.52 % .
Calculated for $C_{30}H_{48}O_3$:	C 78.95;	H 10.53 % .

Further elution with petrol-benzene (1:1) gave another solid, which was crystallised from $CHCl_3$-MeOH to give a pure compound identified

as odollactone (friedelan 3α-hydroxy 27→15α olide) **90**, *M.P.*>320°, $[\alpha]_D$ =-12.14°; IR : 3480 (-OH) and 1758 cm^{-1} (γ-lactone) by comparison with authentic sample. (Co-tlc & Co-IR)

DEHYDRATION of 3β-HYDROXY FRIEDELAN 27→15α-OLIDE **89** *(EPI-ODOLLACTONE)*

2.0 g of epi-odollactone was dissolved in pyridine 10 ml. and 4 ml. of $POCl_3$ added. The mixture was then heated for 4 hours over waterbath and after workup the gummy mass obtained was chromatographed over silica gel column. On elution with petrol-benzene (4:1) a solid was obtained which was crystallised from $CHCl_3$-MeOH, *M.P.*>300°c ; IR : 800 cm^{-1}. (-CH=CH-), gave yellow colour with TNM, identified as 3(4)-dehydro-friedelan 27→15-olide **91**, from ^1H NMR and Mass spectra.

OXIDATION OF 3,4 DEHYDRO ODOLACTONE **91** *WITH SELENIUM DIOXIDE IN t-BuOH CONTAINING HYDROGEN PEROXIDE.*

1.0 g of 3,4 dehydro odolactone **91**, was dissolved in t-butanol and 0.8 g of SeO_2 added followed by H_2O_2 (30% ,4 ml.). The mixture was refluxed for 40 hours and after workup, the gummy product obtained from the neutral ether layer was chromatographed. The column was eluted with following solvents as shown in table-VI.
The alkali layer was acidified like before and since no solid material separated out it was rejected.

TABLE-VI.

	Eluent	Fraction 50 ml each.	Residue on distillation.
1.	petrol	1-5	oil.
2.	petrol-benzene (4:1)	6-10	solid. (0.1 g)
3.	petrol-benzene (1:1)	11-15	nil.
4.	benzene	16-20	nil.
5.	benzene-chloroform	21-28	solid. (0.45 g)

(1:1)

Further elution did not afford any more solid.

Fractions 6-10 were collected and crystallised from $CHCl_3$-MeOH, which was found to be unreacted compound by comparison (CO-tlc & *M.M.P.*) with authentic sample.

Fractions 21-28 were combined and repeatedly crystallised from ethyl acetate-petrol, *M.P.* 270-71°c, identified as friedelan 3β,4α dihydroxy 27→15α olide **92** from spectral studies.

ANALYSIS REPORT.

Found :	C 76.01 ; H 10.24%.
Calculated for $C_{30}H_{48}O_4$:	C 76.27 ; H 10.16%
IR (Nujol) : ν_{max}	3500 and 3440 cm^{-1}. (-OH) fig.**18**.
Mass : m/e	472 (M, 22%), 436, 386, 385 (100), 123. fig. **19**.
^1H NMR : ($CDCl_3$) (δ in ppm.)	0.86, 0.94, 0.96, 0.99, 1.02, 1.05 and 1.21 (7s,21H, 7X t-CH_3) 2.02 (t,1H, J= 3 & 13.5 Hz.) 3.54 (t,1H,J= 3 HZ. 3α-H) 4.34 (t,1H,J= 3 Hz. 15β-H) fig.**20**.
^{13}C NMR :	fig.**21**

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PART-II

ACTION OF N-BROMOSUCCINIMIDE ON PENTACYCLIC TRITERPENOIDS OF LUPANE AND FRIEDELANE SKELETON IN DIMETHYL SULFOXIDE.

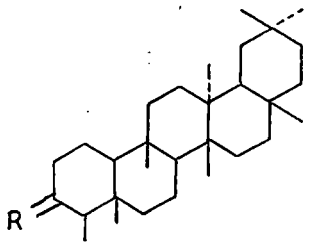
CHAPTER-I

A SHORT REVIEW OF REACTIONS OF N-BROMOSUCCINIMIDE.

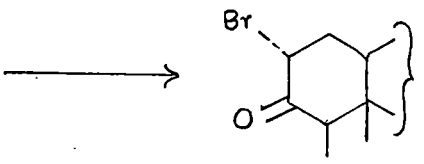
The reagent N-bromo-succinimide(NBS) has been extensively used as an allylic brominating agent since 1919, when Wohl[1] and then Zeigler[2] made a detailed study in this field. The reagent also reacts with olefins to add bromine atom at the double bond and also used for oxidation of allylic methylene to carbonyl functions[3-5] . Triterpenoids undergo a variety of rearrangement reactions with NBS. The author have carried out some reactions of NBS on triterpenoids and it is necessary to give a brief discussion on the previous works of this type of rearrangement reactions.

ALLYLIC BROMINATION AND RELATED REACTIONS:

Corey and Ursprung[6] have reported that friedlin-1 on direct bromination gave 2α-bromofriedlin 2 and bromination of appropriate enol benzoate gave the isomeric 4α-bromofriedlin 3 . They have also prepared a dibromofriedlin 4 by reaction with HBr in $CHCl_3$, which they assigned as 2α, 4α-dibromofriedlin from UV spectra. Djerassi et al[7] reported the formation of 2α,4β-dibromofriedlin 5 by bromination of 2α-bromofriedlin 2 in acetic acid. Stevenson et al[8,9] reported that friedelane 6 was oxidised to friedel 18-ene 7.



1. R=O
6. R=H$_2$



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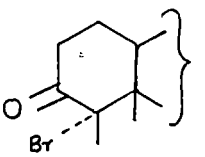

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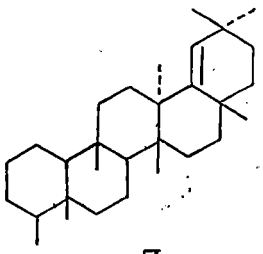

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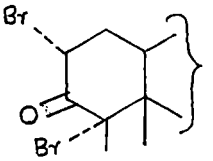

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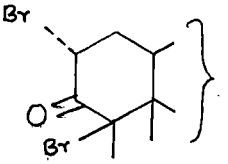
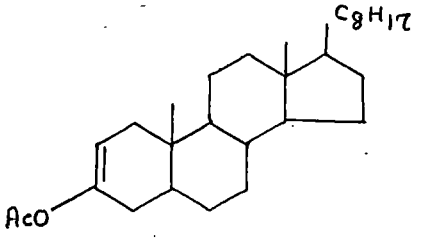


5.

Rubin et al[10] provided an example of allylic bromination with subsequent spontaneous dehydrobromination by reaction of NBS with Δ^2-3-acetoxy-cholestene **8** . This enol actate of cholestanone **9** (ring A/B trans) reacted with NBS in CCl_4 to give a mixture of Δ^1 and Δ^4-cholesten-3-one, **10** and **11** and 2-bromo-cholestan-3-one **12**, the amount of which increased with reaction time at the expense of **10** .



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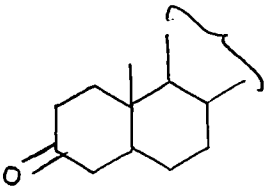

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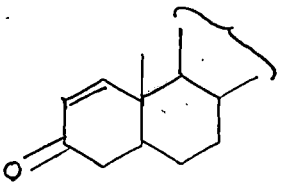

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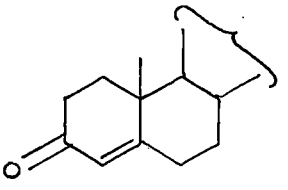

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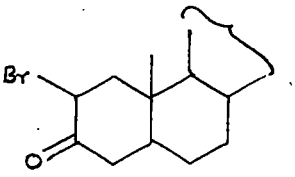
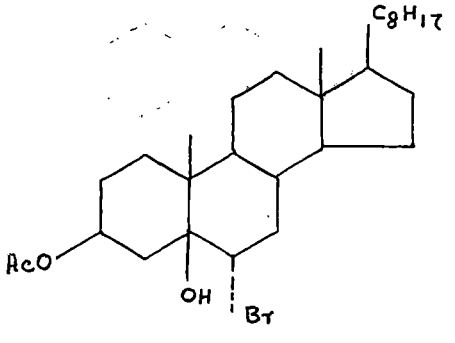


12

Pradhan et al[11] studied the action of NBS on cholesteryl acetate **13** in dimethyl sulfoxide(DMSO) solvent and isolated six different compounds which were identified as 5α-bromo-6-keto cholestan-3β-yl acetate **14**, 6α-bromo-5β-hydroxy coprostan-3β-yl acetate **15**, 5α-hydroxy-6-keto cholestan-3β-yl acetate **16**, 5α,6β-dihydroxy cholestan-3β-yl acetate **17**, 3β,5α-dihydroxy cholestan-6-one **18** and cholestan-3β,5α,6β triol **19** by chemical and spectral (IR, ^{1}H NMR, Mass and ^{13}C NMR) studies. They reported compound **15** for the first time



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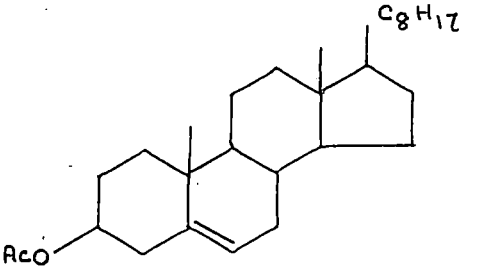

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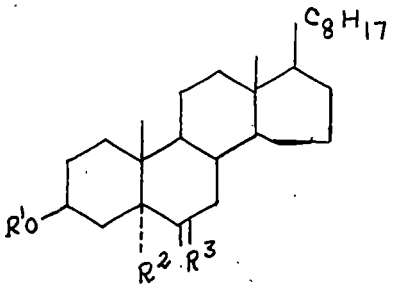


14, R^1 = Ac, R^2= Br and R^3= O.

16, R^1= Ac, R^2= OH and R^3= O.

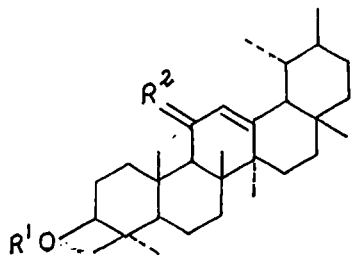
17, R^1= Ac, R^2= OH and R^3=  .

18, R^1= H, R^2= OH and R^3 = O.

19, R^1= H, R^2= OH and R^3 =  .

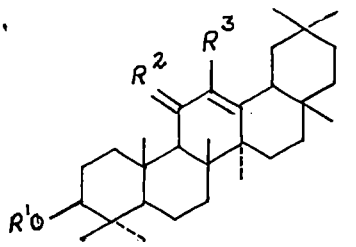
OXIDATION OF ALLYLIC METHYLENE TO CARBONYL GROUP:

Corsano et al[12] reported direct oxidation of the allylic methylene to carbonyl group with NBS in aqueous dioxane solution. Thus 3β-acetoxy-urs-12-ene-11-one **21** was formed in 80% yield from α-amyrin acetate **20**



20, R^1= Ac; R^2= H.

21, R^1= Ac; R^2 = O.



22, R^1= Ac; R^2= H_2; R^3= H

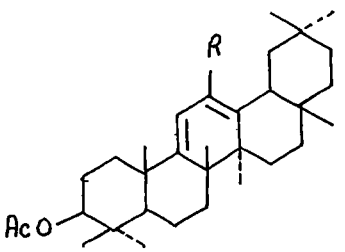
23, R^1= Ac; R^2= O; R^3 = H

24 R^1= Ac; R^2= OH; R^3= H

25, R^1 = Ac; R^2= OMe; R^3= H

26, R^1= Ac; R^2= OAc; R^3= H

27, R^1= Ac; R^2= OH; R^3= Br.

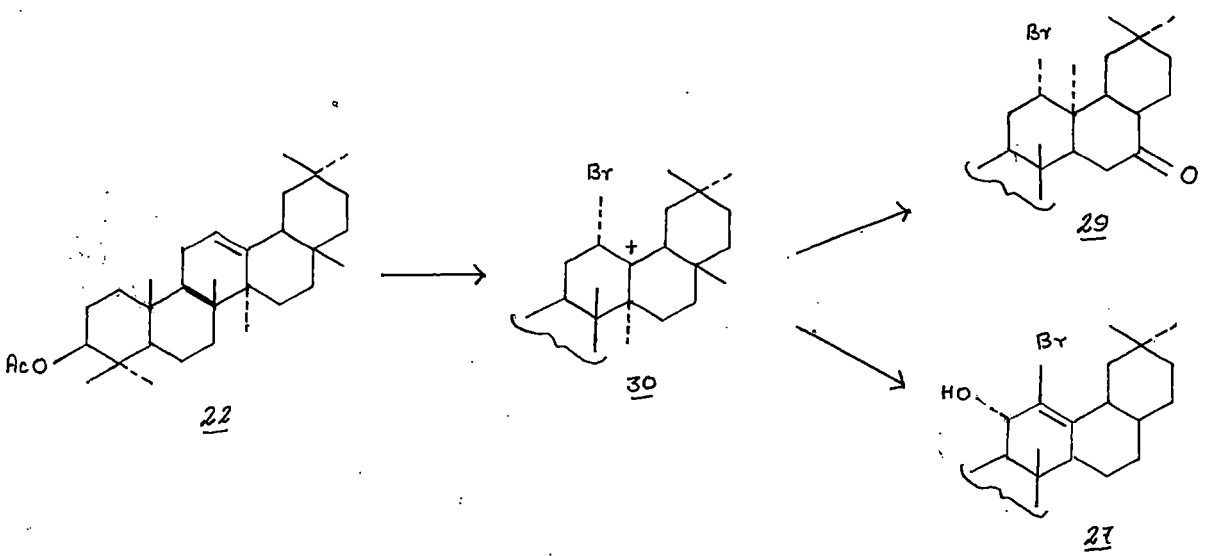


28, R=H.

Finucane et al[13,14] reported an improved method for the direct oxidation of the allylic methylene to carbonyl functions by the action of NBS and simultaneous irradiation with visible light. They claimed

that when trisubstituted olefins containing an allylic methylene group were treated with NBS in aqueous dioxane followed by irradiation with visible light, α,β- unsaturated ketone were formed in high yield. Finucane et al treated β-amyrin acetate 22 with NBS in aqueous dioxane in a typical ambient light experiment as described by Corsano et al[12]. They isolated starting material, 3β-acetoxy-olean-12-ene-11-one, bromo compound and 3β-acetoxy- olean-12-ene-11α-ol, 24. Oxidation of the latter 24 with chromium trioxide in acetone afforded 3β-acetoxy--olean-12-ene-11-one 23.

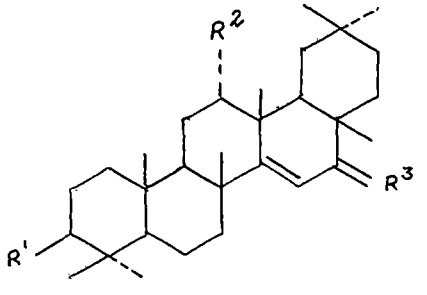
In another experiment,the products were isolated by chromatography over alumina and yielded β-amyrin acetate 22, 3β-acetoxy-olean-12-ene-11-one 23,bromo compound and polar material. The polar fraction on elution with methanol was acetylated and on rechromatography gave 11α-methoxy-olean-12-ene-3β-yl acetate 25 together with smaller amount of 11α-ol 24, and olean-9(11), 12-diene-3β-yl acetate 28 and trace of 3β,11α-diacetate 26. The fractions containing bromo compounds was resolved by chromatography over alumina and fractionally crystallised into two components. the major product was identified as 3β-acetoxy 12-bromo olean-12 ene-11-ol 27,the minor component of the mixture of bromo compound was identified as 12α-bromo-16-one 29. The mechanism proposed for the formation of 27 and 29 suggested that the initial α-face attack on β-amyrin acetate 22 at C-12,would lead to a carbonium ion 30. Elimination of a proton from C-12 followed by allylic hydroxylation would than lead to 27. Alternatively, migration of 14α-methyl group to C-13, elimination of a proton from C-15,and subsequently allylic oxidation would give 29.

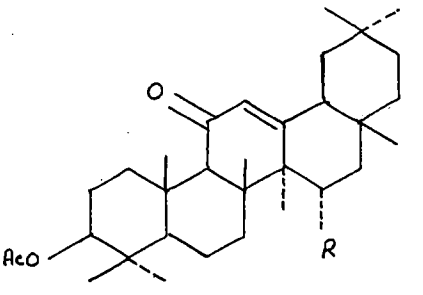


22 30 29 27

Thomson et al[14] carried out oxidation of taraxeryl acetate 31 by following the method of Corsano et al[12] and obtained two major products to which the assigned structure of 16-oxo taraxeryl acetate 32 and 16β-hydroxy taraxeryl acetate 33.
Treatement of 33 with chromic acid in acetone gave the unsaturated ketone 32. The workers also carried out the reaction on 31 by the method described for β-amyrin acetate,which resulted in the formation of 12α-bromo-taraxer-14-ene-16-one 34.

Oxidation of taraxeryl acetate with NBS in aqueous dioxane[13] for 5 hours in presence of $CaCO_3$ in visible light gave a compound 35 the structure of which was established as 11-keto-15-bromo β- amyrin acetate,which in turn yielded a halogen free compound 36 on treatment with Zn-dust in AcOH. Its structure was established as β-amyrenonyl acetate.

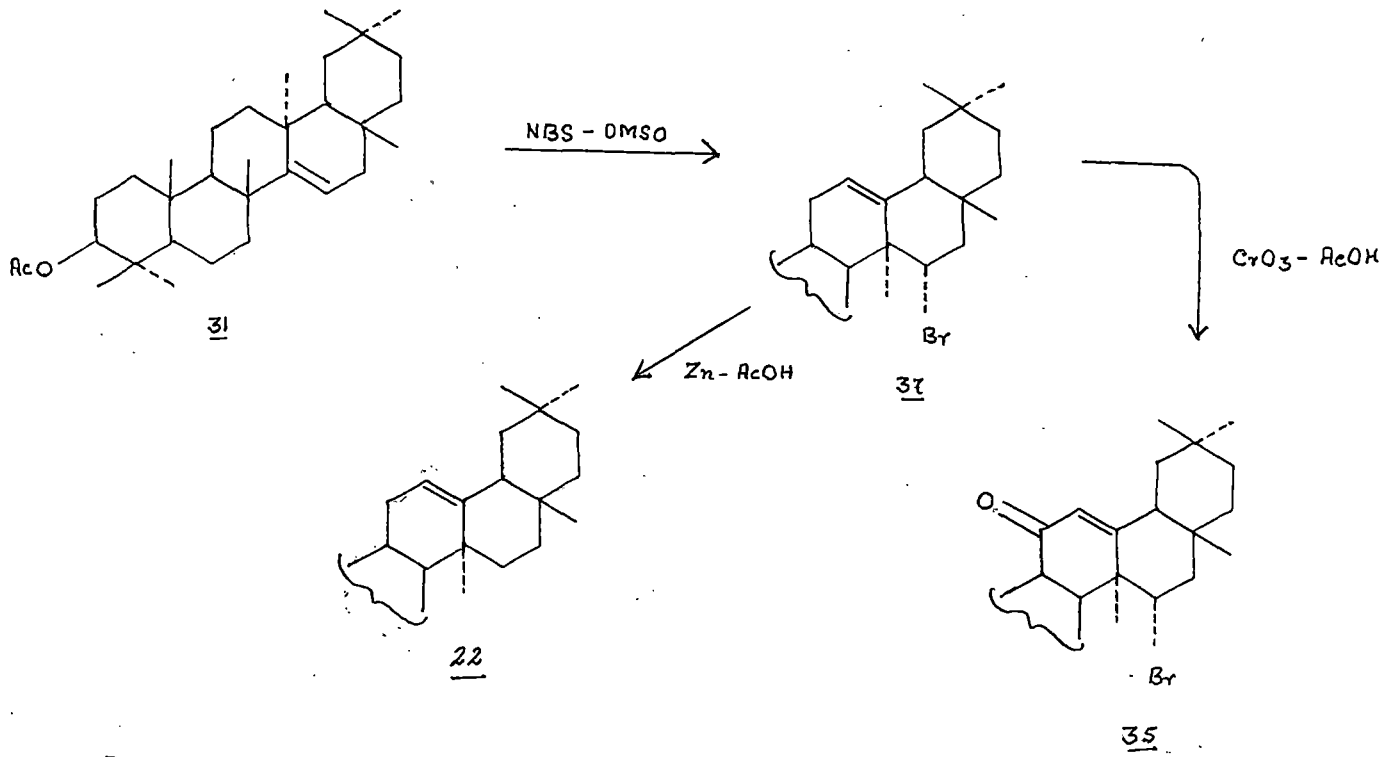




31, R^1= OAc; R^2= H; R^3= H_2
32, R^1=OAc; R^2= H; R^3= O.
33, R^1= OAc; R^2=H; R^3= 
34, R^1= OAc; R^2 = Br; R^3= O

35, R= Br
36, R= H

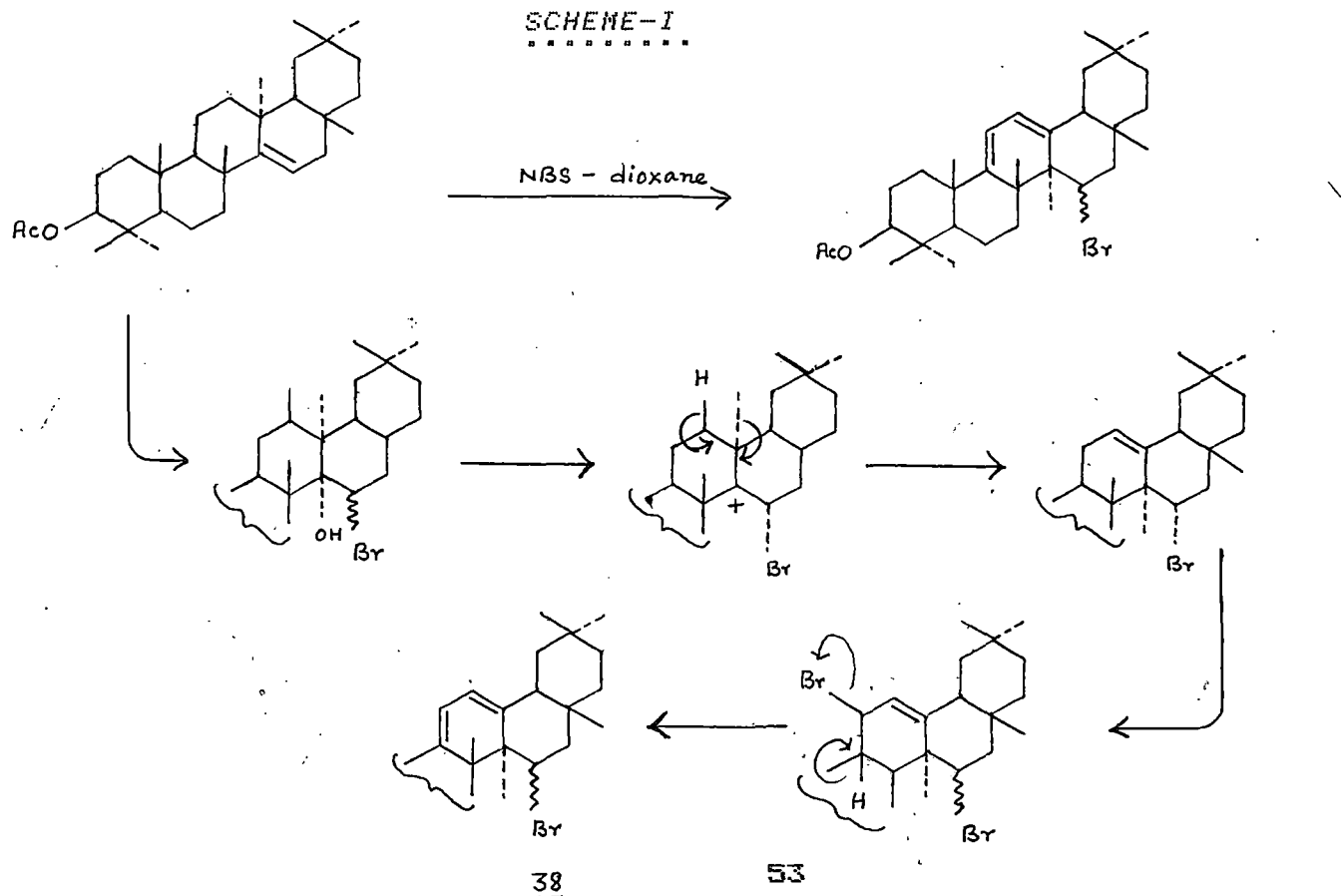
Khastgir et al[15] carried out the oxidation of taraxeryl acetate 31 by the method of Dalton[16] using NBS in DMSO solvent. Treatment of taraxeryl acetate 31 with aqueous DMSO in $CHCl_3$ and NBS in dark afforded a solid 37. The compound 37 on treatment with Zn-acetic acid yielded β-amyrin acetate 22. The Br-atom at 15 position of 37 would be expected to have the same stereochemistry as in the case of product from NBS aqueous dioxane oxidation method. Compound 37 on oxidation with CrO_3-AcOH[17] gave 35 identical with the product obtained from NBS aqueous dioxane oxidation method.



31 37 22 35

The second compound devoid of bromine was identified as 16- oxo taraxeryl acetate 32. The third product was found to be 38. The mechanism for the formation 38 was proposed as in scheme-I.

SCHEME-I

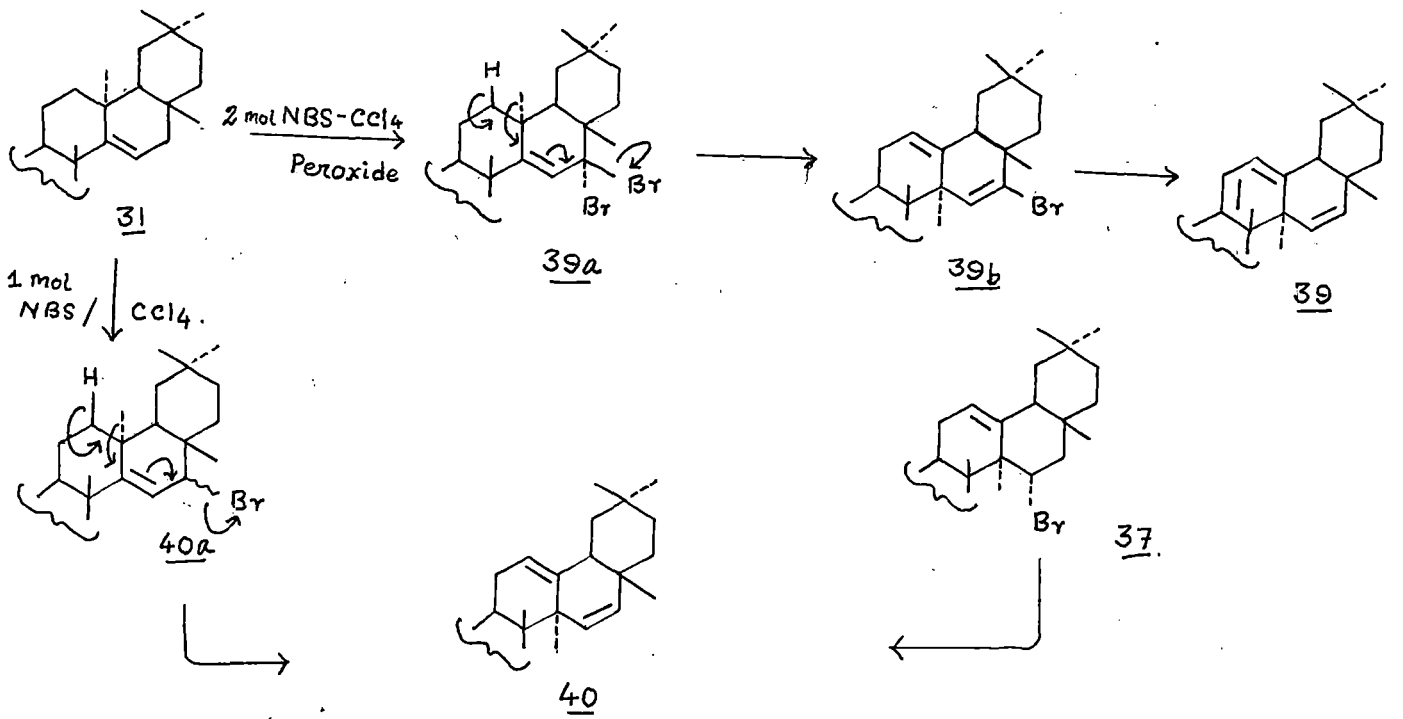


38 53

Khastgir et al[15] also studied the reaction of taraxeryl acetate 31 with 2-moles equivalent of NBS in CCl_4 using light for three hours and isolated a product, which was assigned the structure 39. When the same reaction was carried out with one mole equivalent of NBS, it afforded a halogen free product of structure 40, identical to that obtained by dehydrobromination of 37.

The mechanism for the formation of 40 and 39 was proposed in scheme -II.

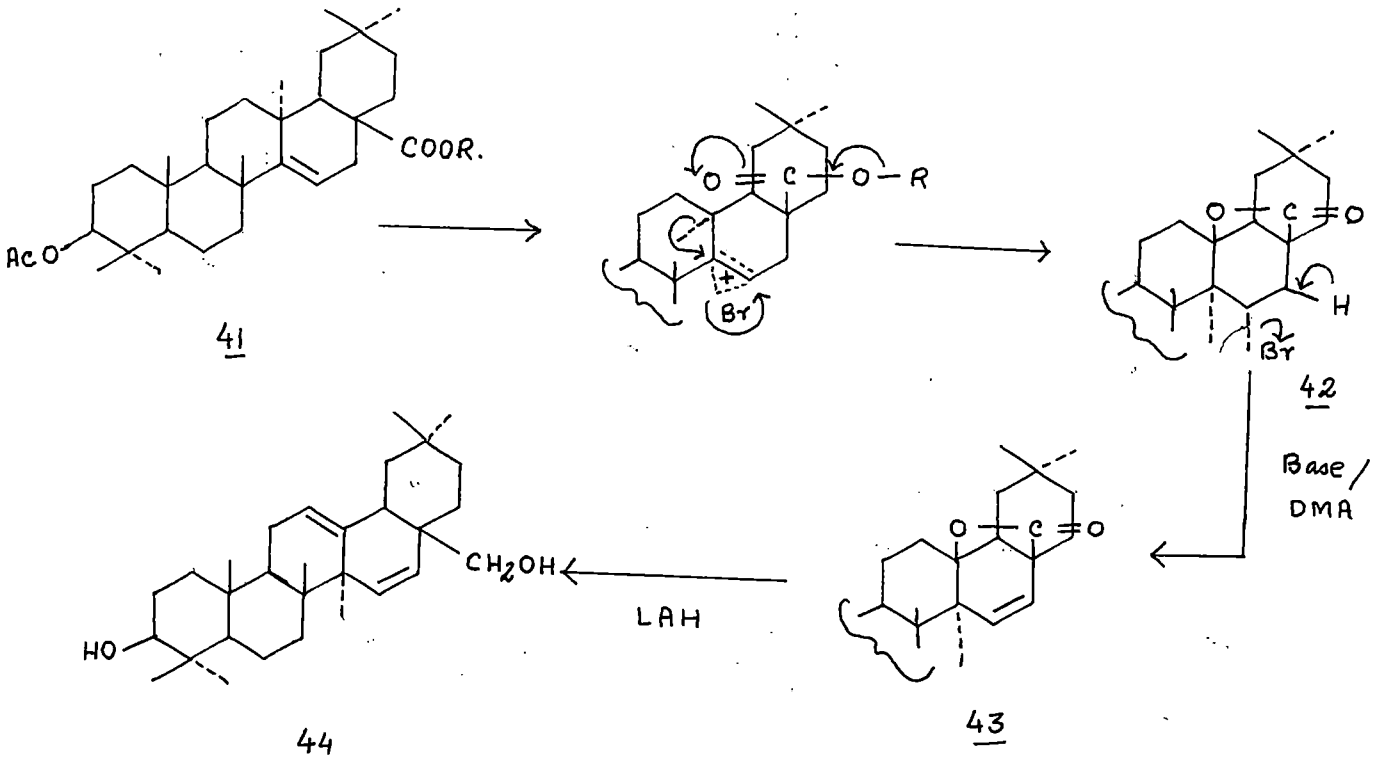
SCHEME-II



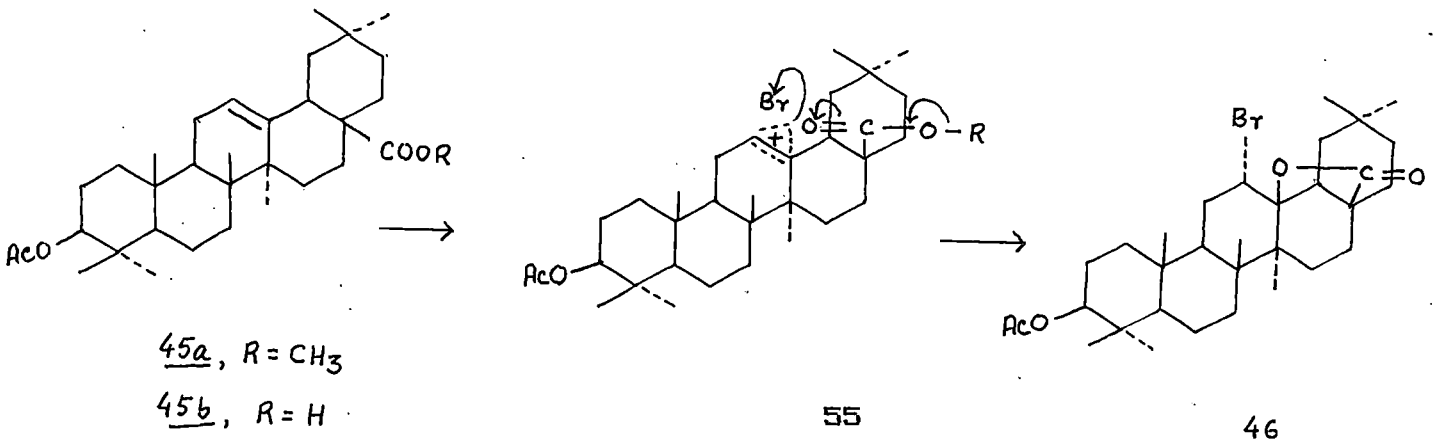
Pradhan et al[18] carried out the reaction of NBS on triterpenoid acids and esters. They studied the reactions of methyl acetyl aleuritolate 41 with NBS in DMSO in the dark for 12 hours and isolated a bromo-lactone 42. The structure of the bromo-lactone was confirmed from the fact that dehydrobromination with dimethyl aniline afforded 15,16-dehydrolactone 43 which on LAH reduction furnished aegiceradiol 44.

The mechanism of formation of **42** involved the attack of bromonium ion from NBS in DMSO at the double bond. Bromine being a bulky atom ultimately assumed the equitorial position so as to have the minimum strain and steric interaction. The next step involved concerted migration of the C-13 methyl to the C-14 position and elimination of the methoxy methyl to form the 28 → 13-olide **42**. The mechanism is shown in the following scheme-III

SCHEME-III



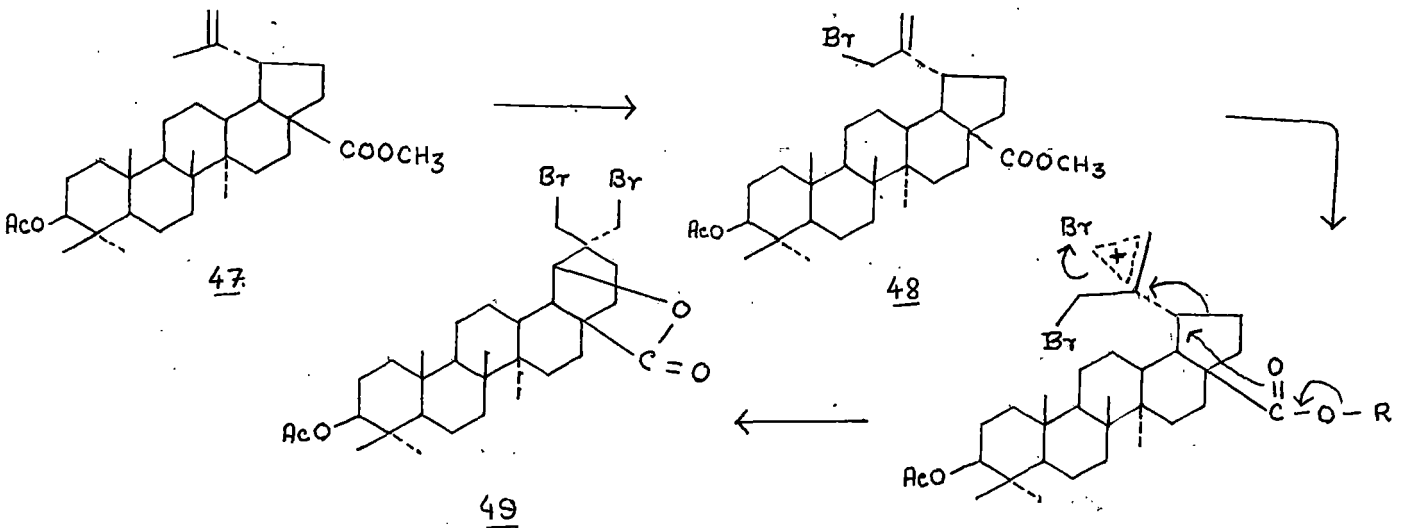
Methyl acetyl oleanolate **45a** and 3β-acetyl oleanolic acid **45b** under the same condition afforded the bromolactone **46** which was found to be identical with 12α-bromo oleanan-28 → 13-olide.[19]



Methyl 3β-acetyl betulinate **47** on similar reaction with NBS in DMSO afforded two different bromo compounds. The less polar one was identified as methyl 30-bromo-3β-acetyl betulinate **48**. The more polar fraction was dibromo-lactone **49**.

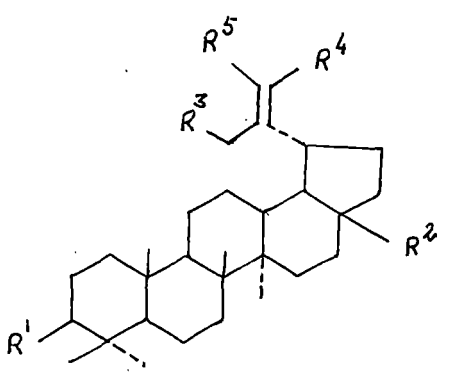
The proposed mechanism of formation of **48** and **49** is shown below in the scheme-IV.

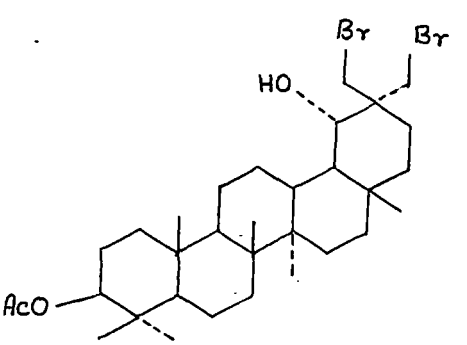
SCHEME-IV



47 48 49

Recently Pradhan et al[20] reported the action of NBS on lupenyl acetate **50** in DMSO and isolated four different compounds which were 30-bromo lupenyl acetate **50a**, 29(E-Z)-bromo lupenyl acetates **50c** & **50d** and 29,30-dibromo 18-iso-oleanan-19α-hydroxy 3β-yl acetate **51**.





51.

50, R^1 = OAc; R^2 = CH_3; R^3 = R^4 = R^5 = H
50a, R^1 = OAc; R^2 = CH_3; R^3 = Br; R^4 = R^5 = H
50c, R^1 = OAc; R^2 = CH_3; R^4 = Br; R^3 = R^5 = H
50d, R^1 = OAc; R^2 = CH_3; R^5 = Br; R^3 = R^4 = H

Compound **50a** and mixture of **50c** & **50d** with NBS in DMSO containing water afforded 30-oxo lupeol **50k** and 20(E-Z)-bromo lupeol **50l** & **50m** respectively.

$$\underline{50a} \;/\; (\underline{50c} \;\&\; \underline{50d}) \xrightarrow[\text{water}]{\text{NBS-DMSO}} \underline{50k} + \underline{50l} + \underline{50m}$$

50k, $R^1 = OH$; $R^2 = CH_3$; $R^3 = O$; $R^4 = R^5 = H$
50l, $R^1 = OH$; $R^2 = CH_3$; $R^5 = Br$; $R^3 = R^4 = H$
50m, $R^1 = OH$; $R^2 = CH_3$; $R^4 = Br$; $R^3 = R^5 = H$

Compound **50a** on alumina afforded 30-hydroxy lupenyl acetate **50h** and 30-hydroxy lupeol **50i**

50h, $R^1 = OAc$; $R^2 = CH_3$; $R^3 = OH$; $R^4 = R^5 = H$
50i, $R^1 = R^3 = OH$; $R^2 = CH_3$; $R^4 = R^5 = H$

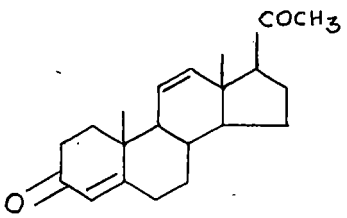
(A detailed report of this investigation has been published in Indian Journal of Chemistry, 1991, pages 32-37, a reprint of which is enclosed in appendix-1.)

ALLYLIC HYDROXYLATION BY N-BROMOSUCCINIMIDE

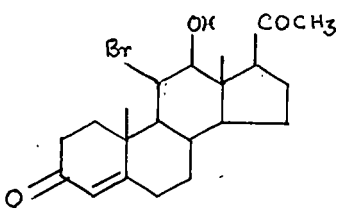
The NBS may be used for the introduction of allylic hydroxyl group. The method is indirect and usually involves allylic bromination and conversion of the resulting bromide into alcohol via the formation of formate or acetate. Thus 3-p menthene 5-yl bromide was prepared from 3-p methene using NBS in $CHCl_3$ and UV light. The bromide was converted to 3-p menthene 5-yl formate by sodium formate and the crude ester on treatment with methanolic sodium carbonate gave *dl*-trans 3-p menthene 5-ol[21].

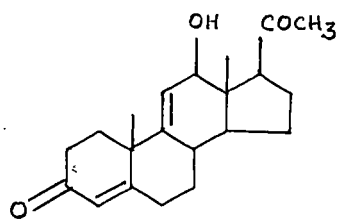
A mixture of *cis* (38%) and *trans* (62%) *Cyclodecene* formed the bromide, which on reaction with silver acetate in glacial acetic acid gave the

crude acetate from which 2-cyclodecen-1-ol was obtained on treatment with methanolic hydroxide[22]. An example of hydroxylation of steroids is illustrated by the transformation of 11-dihydro progesterone 52 to give $\Delta^{4-9(11)}$ pregenadien 12α-ol 3,20 dione[23] 53.



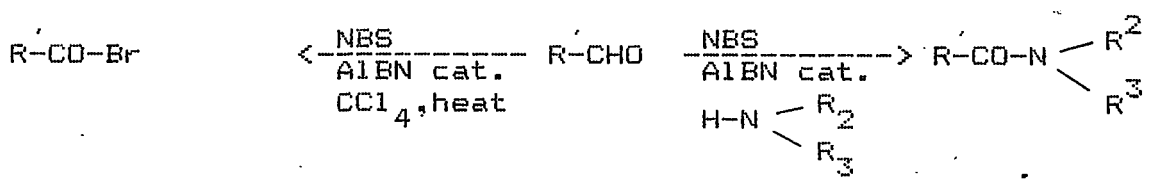
52





53

Recently Marks et al[24] reported the conversion of aldehydes directly into acid bromides and amides by action of NBS in presence of catalytic amount of AIBN as radical initiator.



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

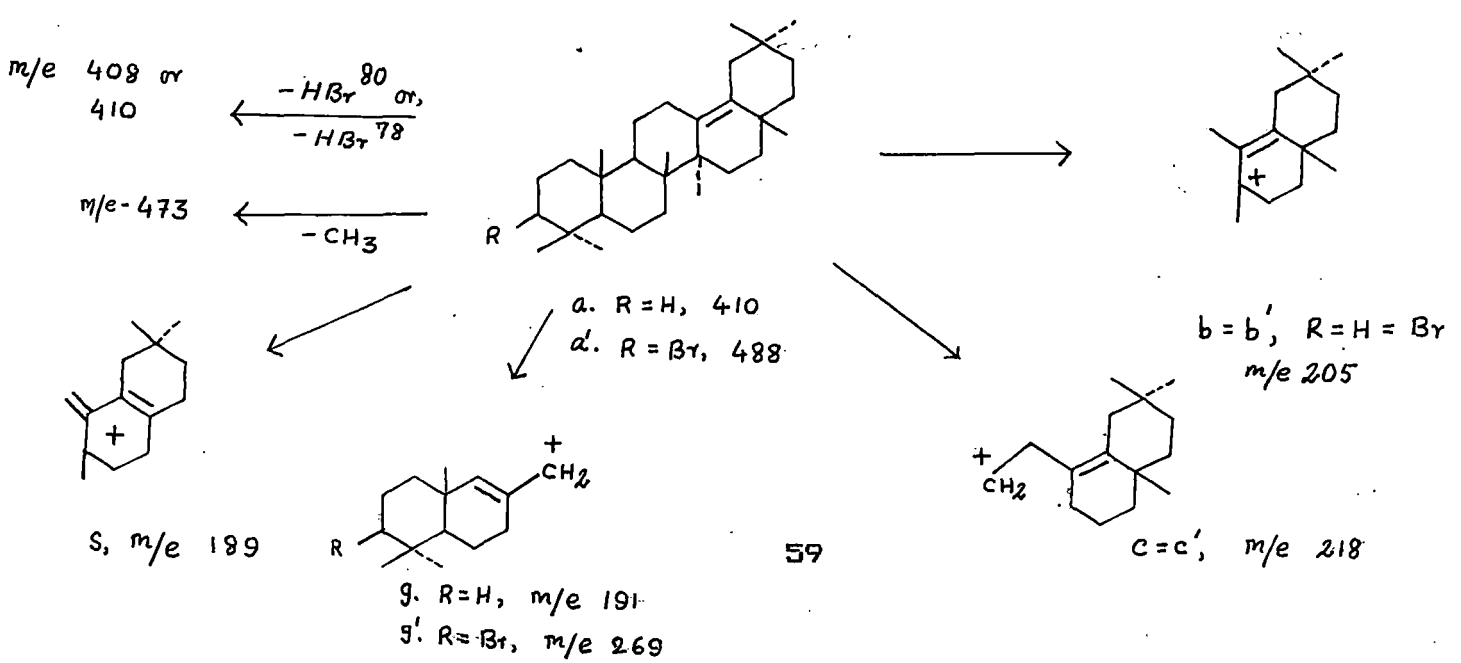
Friedel-3(4)-ene **54** was dissolved in small volume of chloroform and dimethyl sulfoxide was added followed by N-bromosuccinimide. The mixture was then kept in dark for 24 hours and the product obtained was chromatographed over silica gel column. On elution with solvents, two compounds A and B were 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 $C_{30}H_{49}Br$

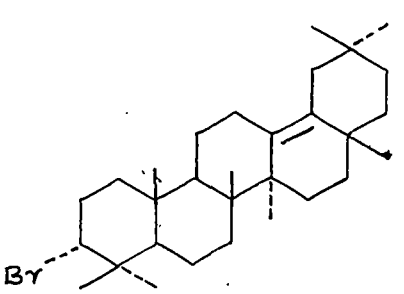
The ^1H NMR (fig.2) resonance signals are recorded in tabular form below :-

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,

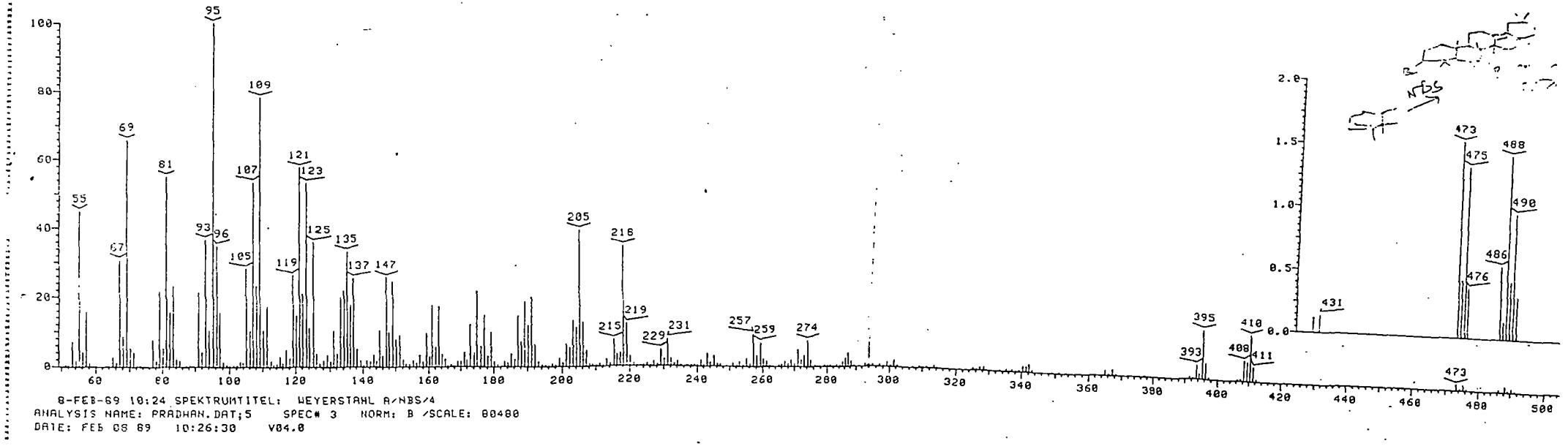


Fig.1. Mass spectrum of 3α- bromo-olean-13(18)-ene, 55.

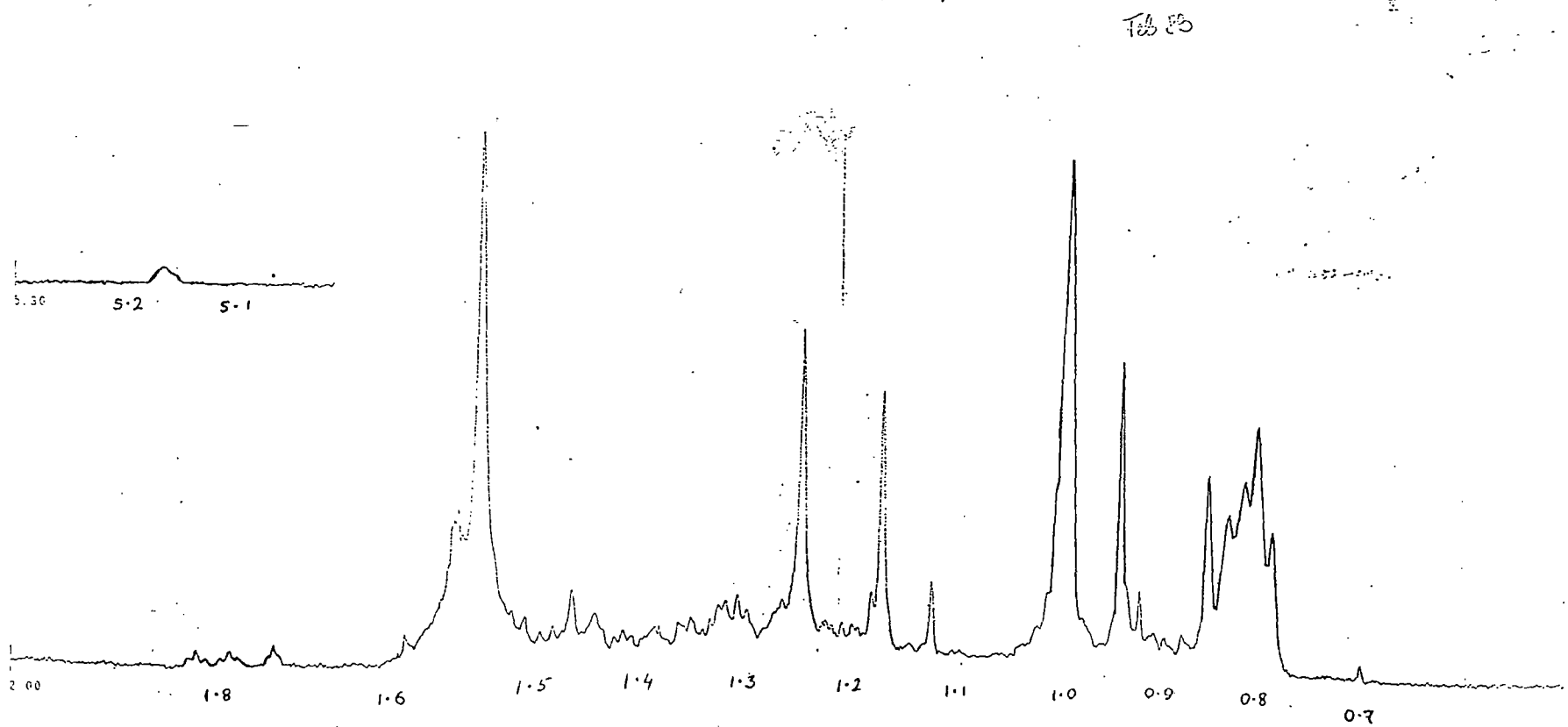
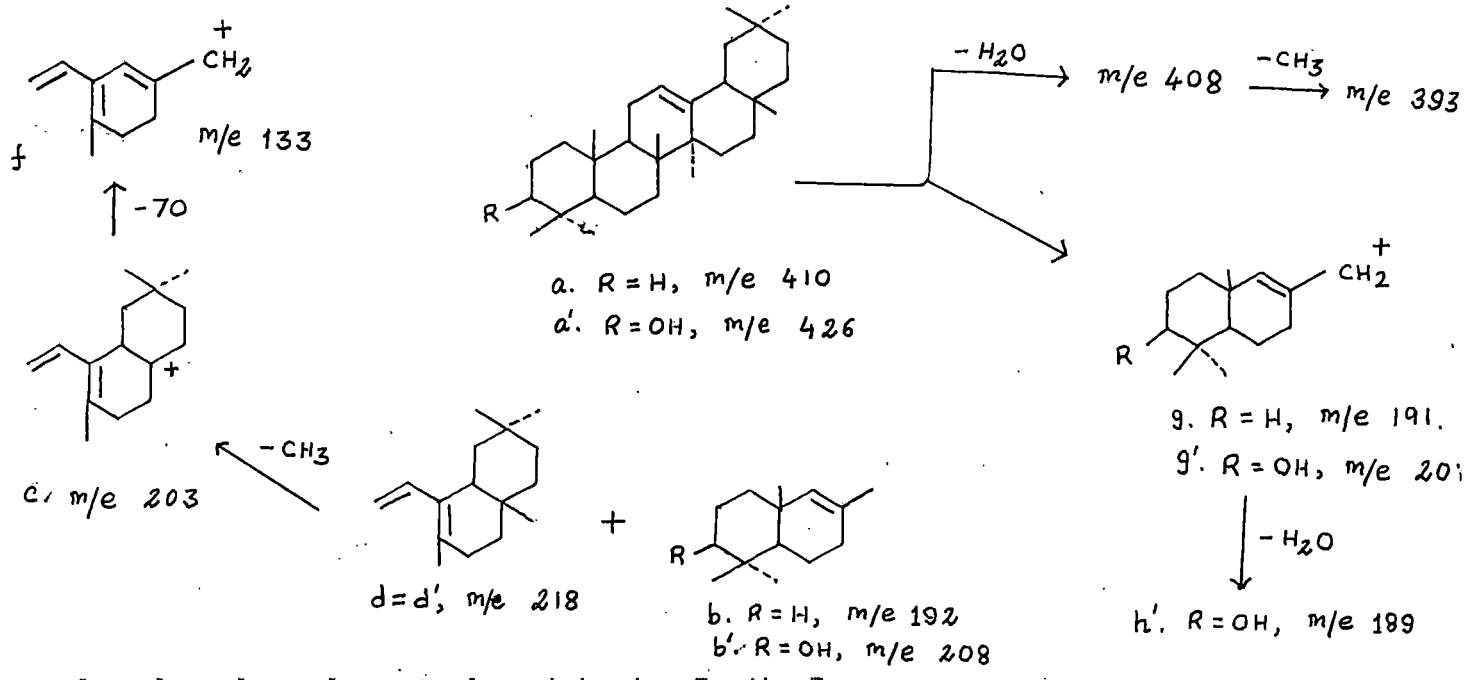


Fig.2. ^{1}H NMR spectrum of 3α- bromo-olean-13(18)-ene, 55.

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 $C_{30}H_{50}O$.

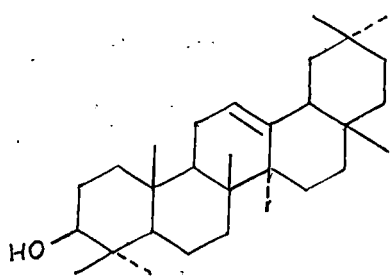
The ^1H NMR (fig.5) signals are recorded below in table-II.

TABLE-II

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

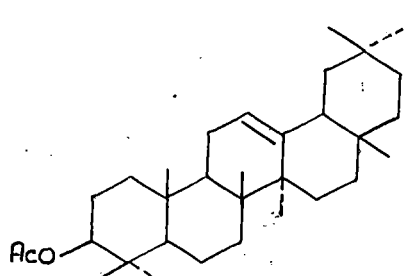
0.82	3	"	8 tertiary
0.87	3	"	methyls.
0.94	3	"	
0.99	3	"	
1.06	6	"	
4.08	1	broad singlet like.	equatorial methine proton.
5.53	1	triplet (J= 3 & 7 Hz)	olefinic proton.

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,

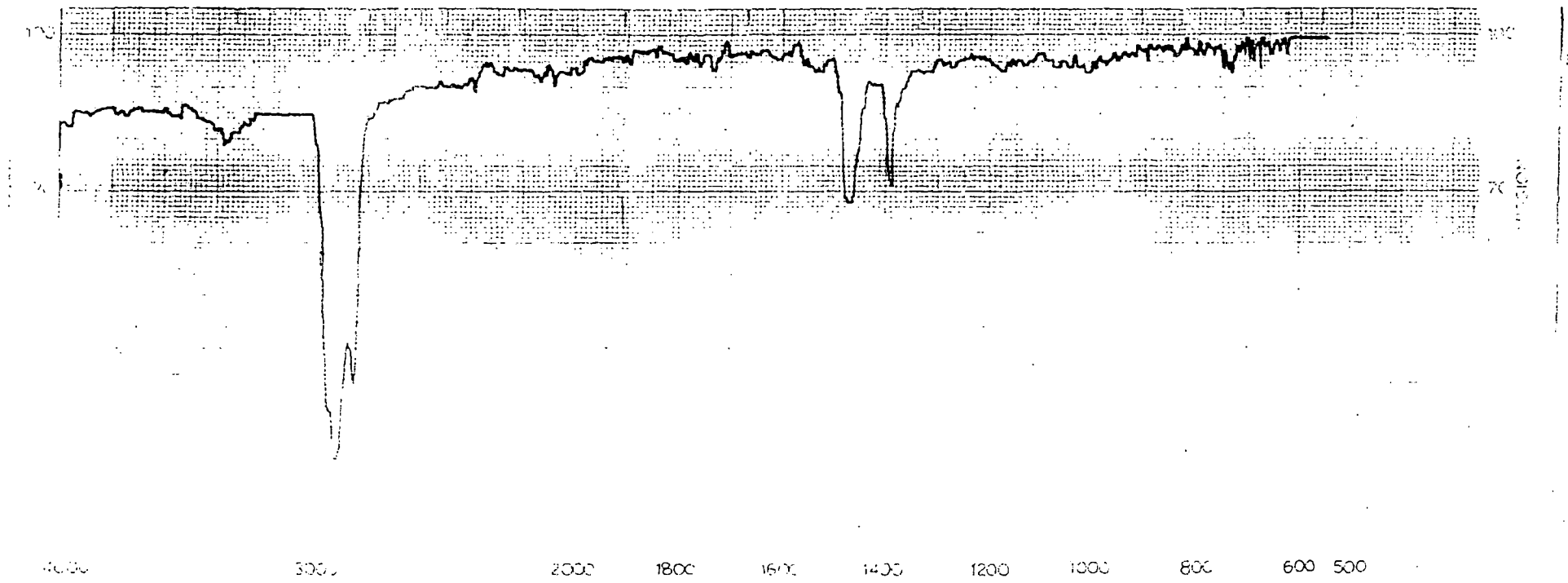


Fig.3. IR spectrum of 3β-hydroxy-olean-12(13)-ene, 56a.

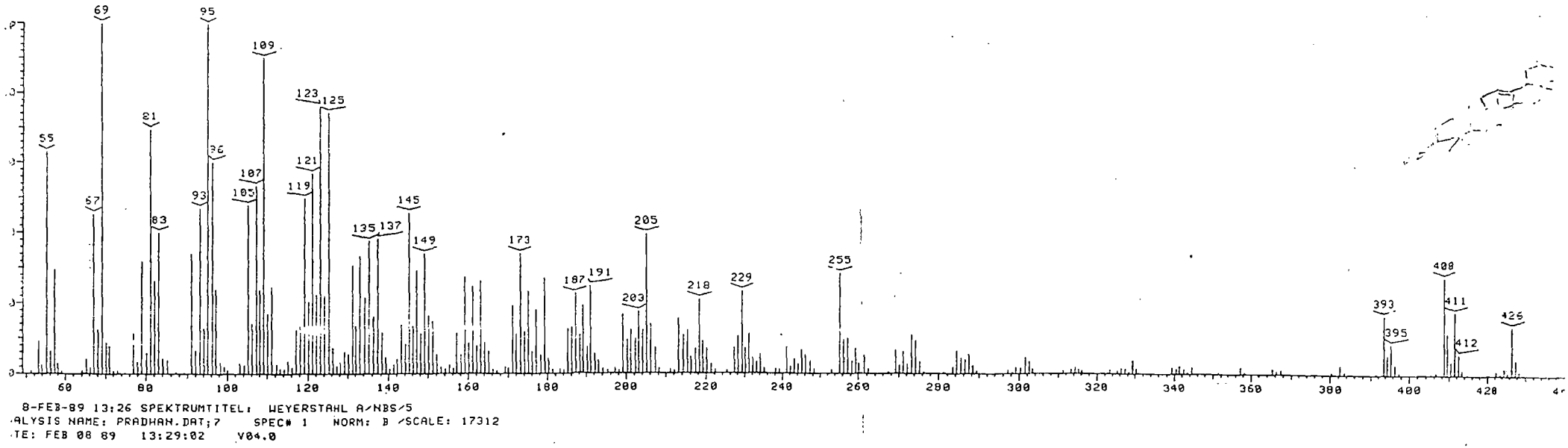


Fig.4. Mass spectrum of 3β-hydroxy-olean-12(13)-ene, 56a.

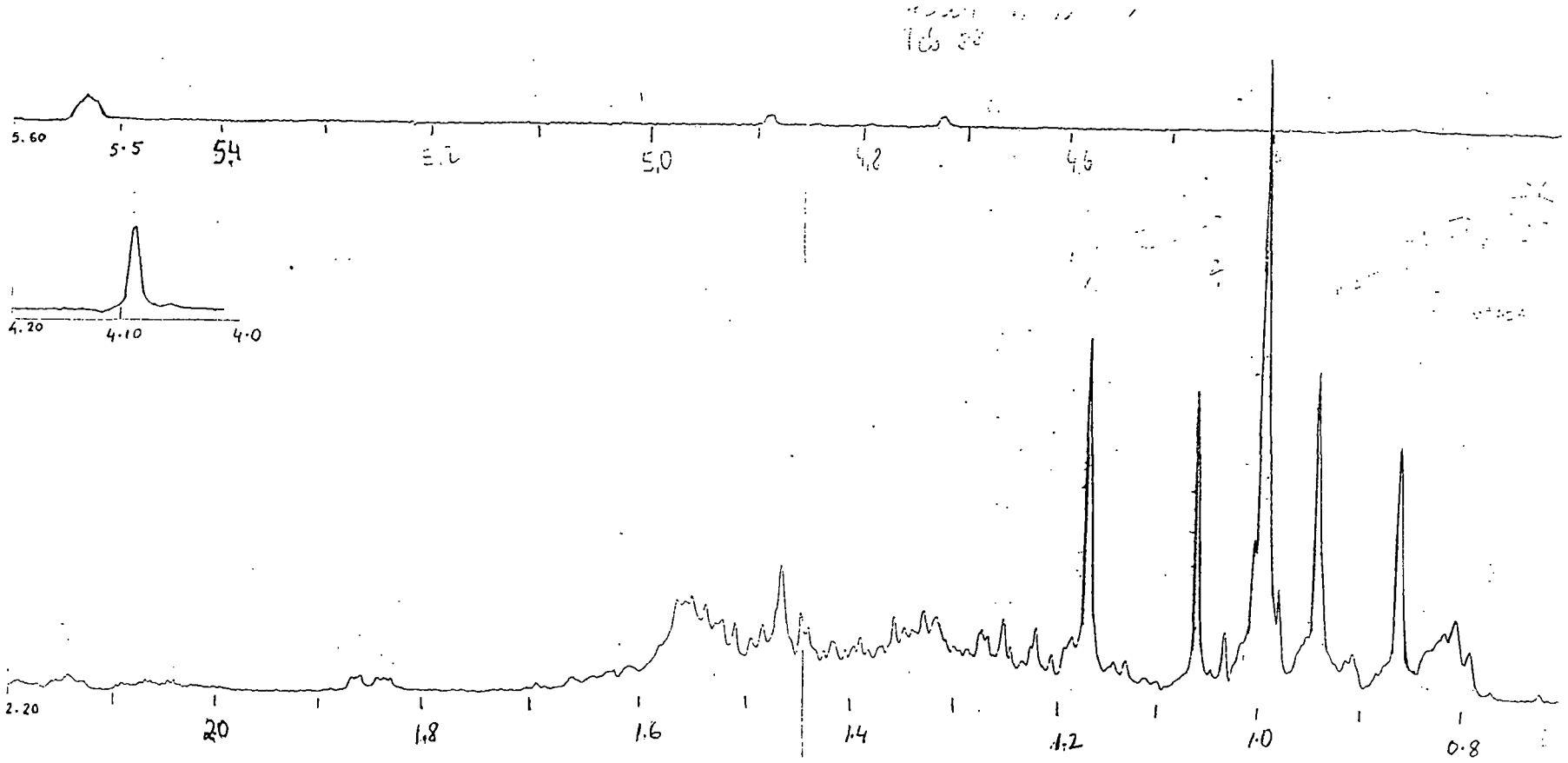
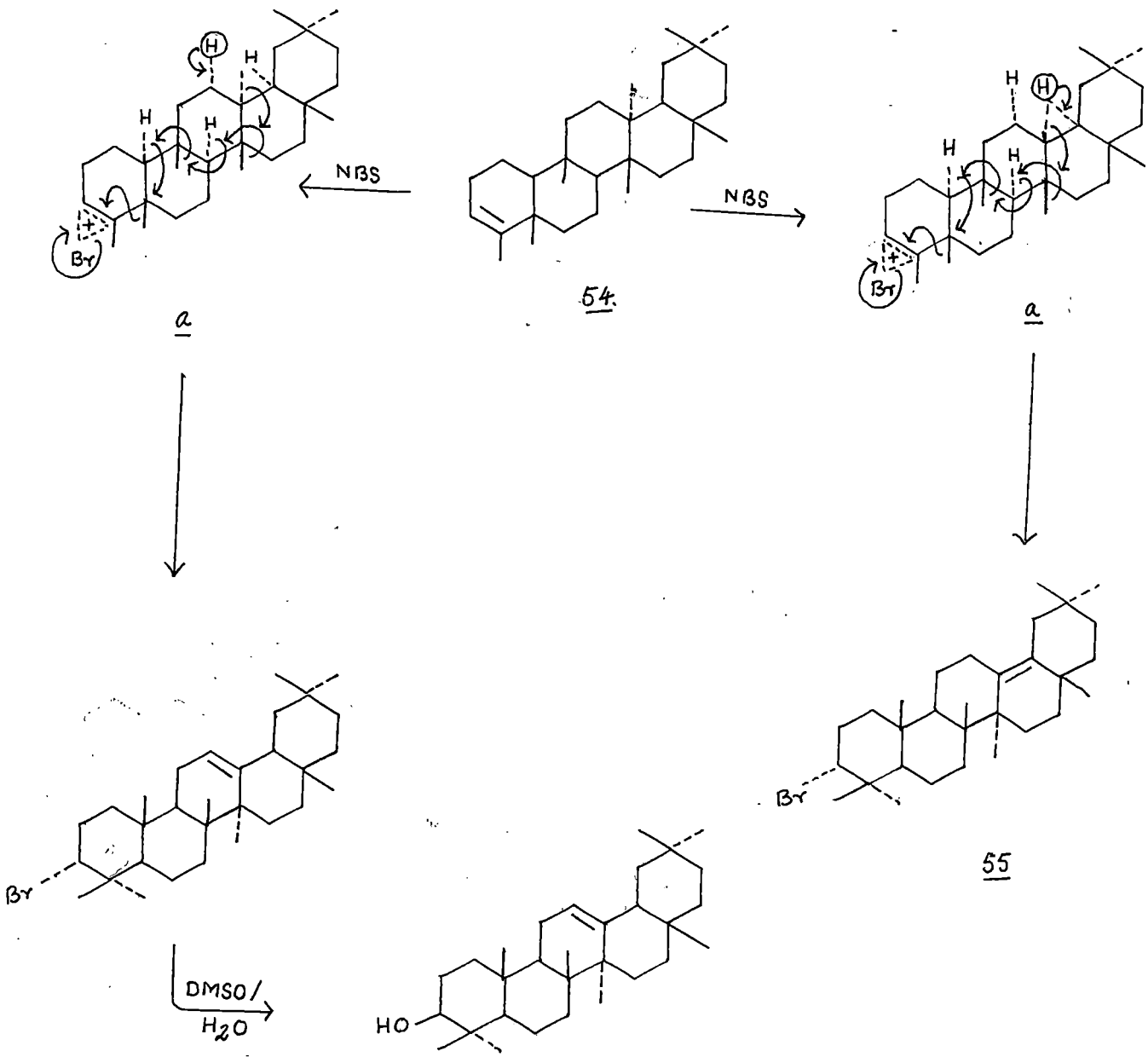


Fig.5. ^{1}H NMR spectrum of 3β-hydroxy-olean-12(13)-ene, 56a.

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.

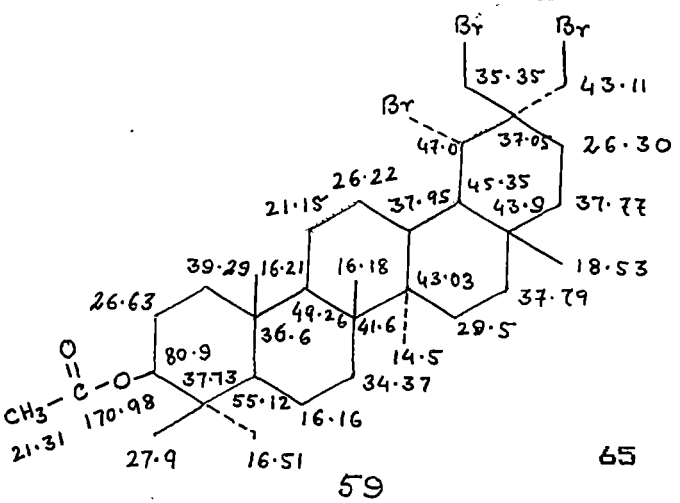
Chemical shift (δ in ppm)	No. of proton	Multiplicity	Assignment.
0.84	3	singlet	
0.85	3	"	
0.86	3	"	

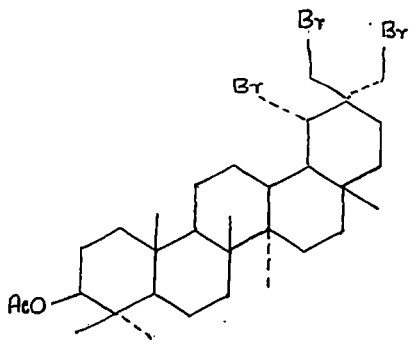
0.94	3	"	6X t-CH_3
0.95	3	"	
1.06	3	"	
2.05	3	singlet	$-OCOCH_3$
3.5-3.9	2	AB_q (J=10 Hz)	$-CH_2Br$
3.8-4.6	2	AB_q (J=11.5 Hz)	$-CH_2Br$
4.48	1	multiplet	$-C_3-\alpha H$.
4.24	1	doublet	$-C_{19}-\beta H$.

.....

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

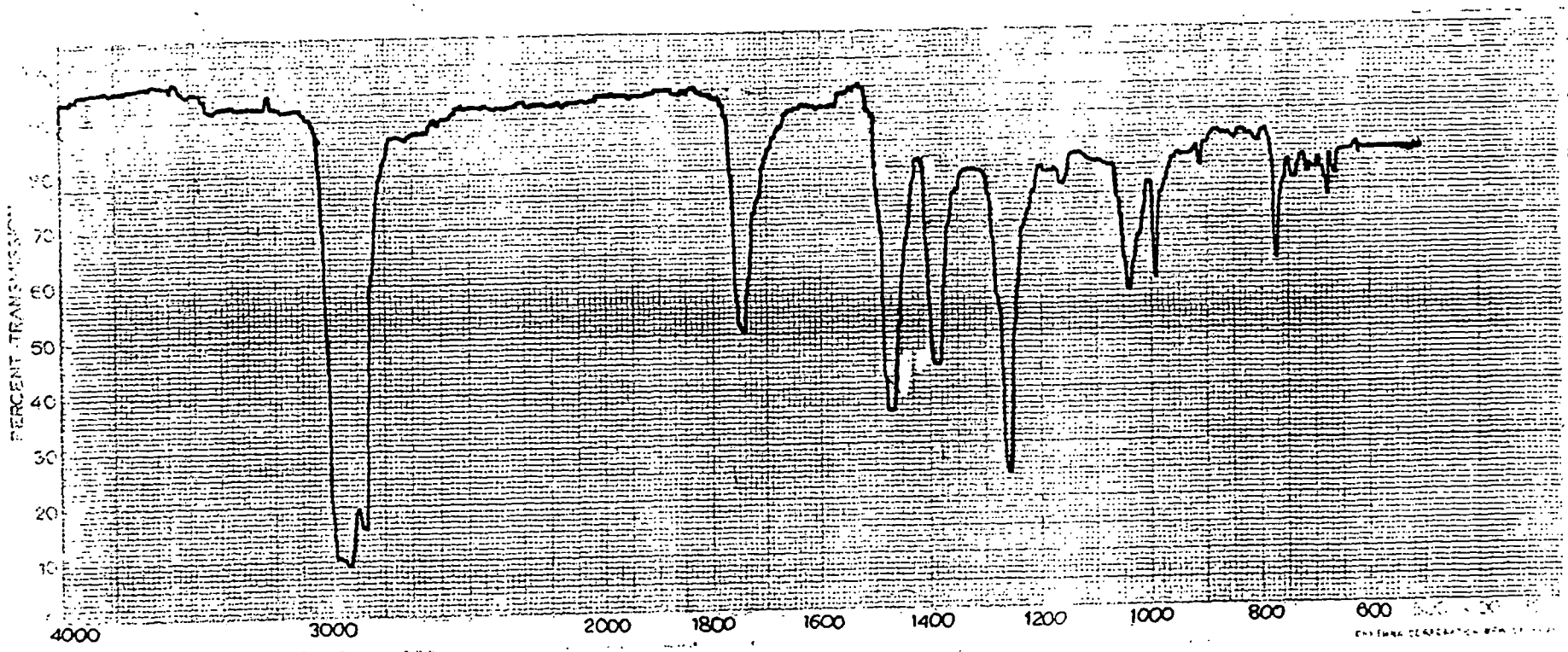


Fig. 6, IR spectrum of 3β-acetyl 19α,29,30 tribromo Oleanane, 59.

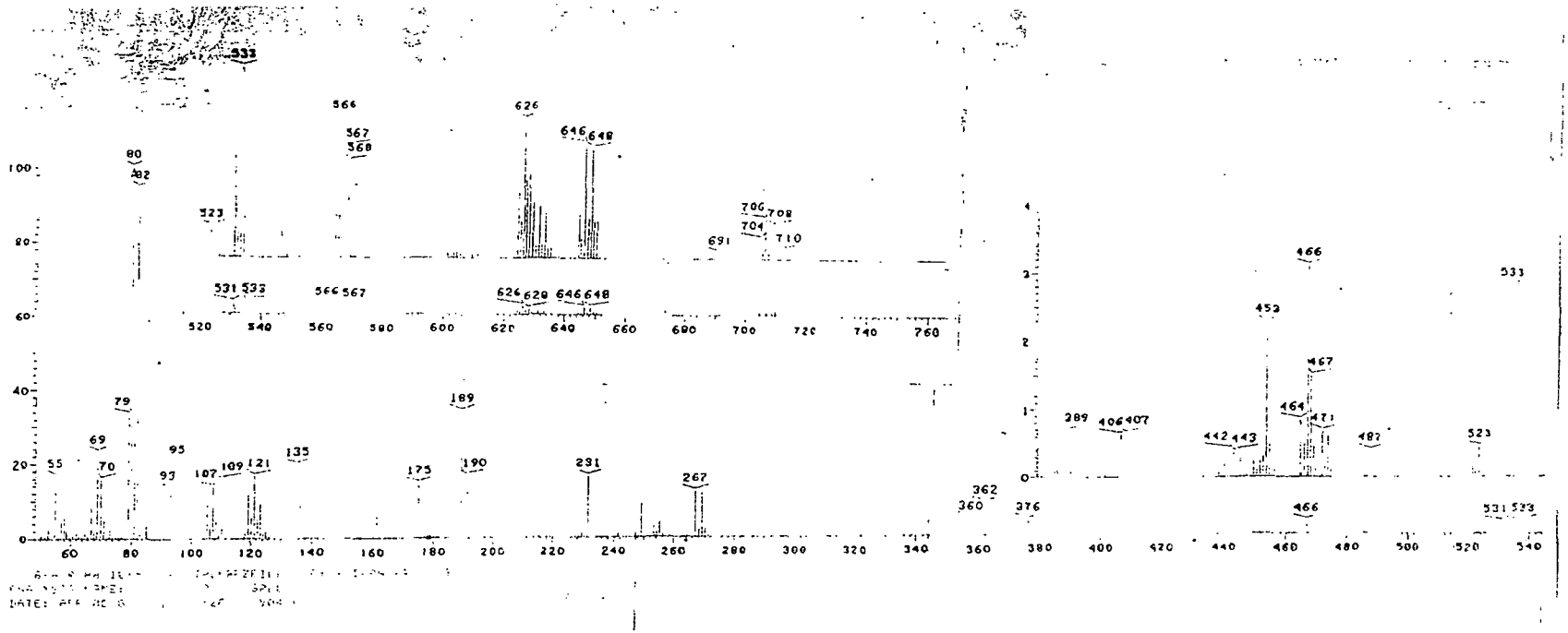


Fig. 7, Mass spectrum of 3β-acetyl 19α,29,30 tribromo Oleanane, 59.

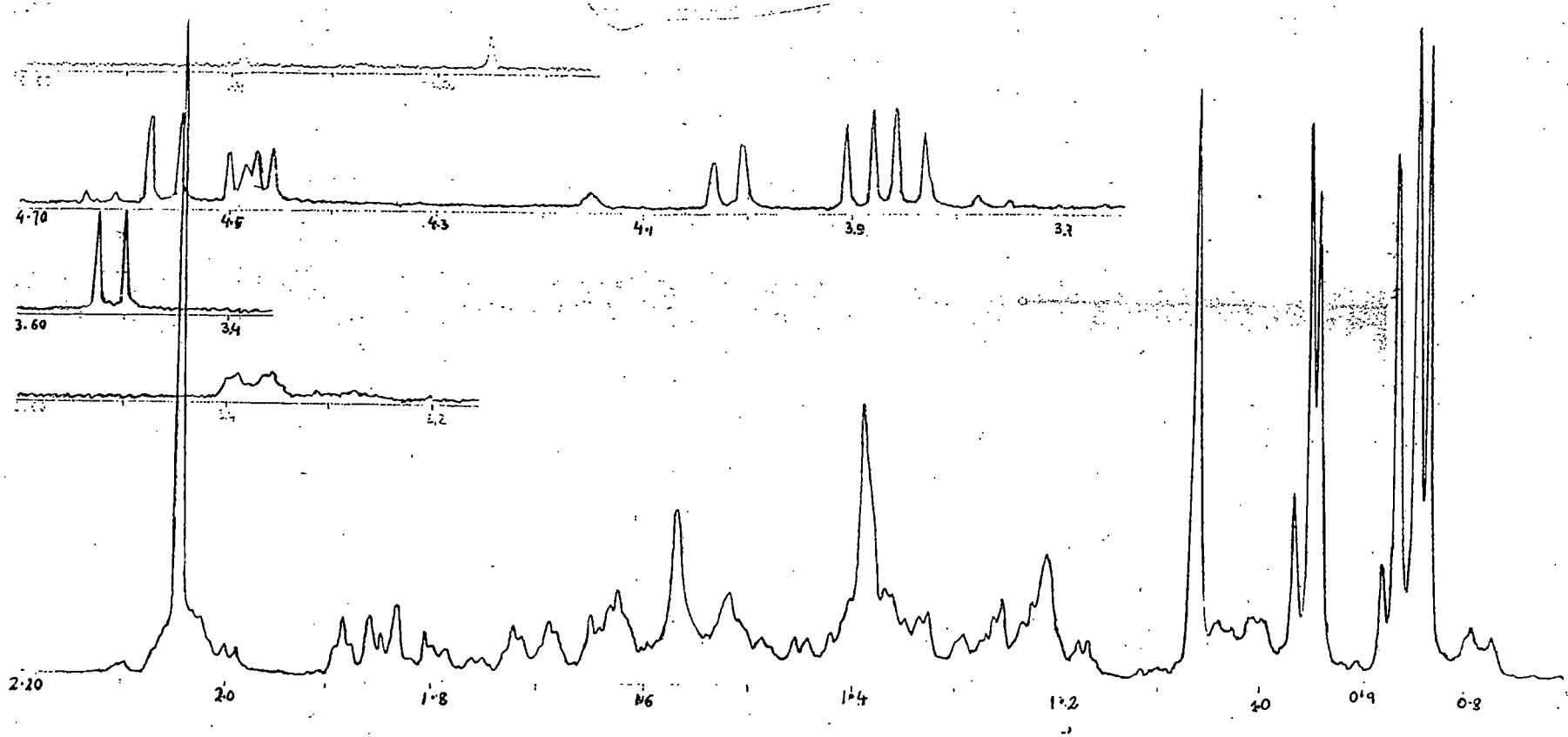


Fig. 8, ^{1}H NMR spectrum of 3β-acetyl 19α,29,30 tribromo Oleanane, 59.

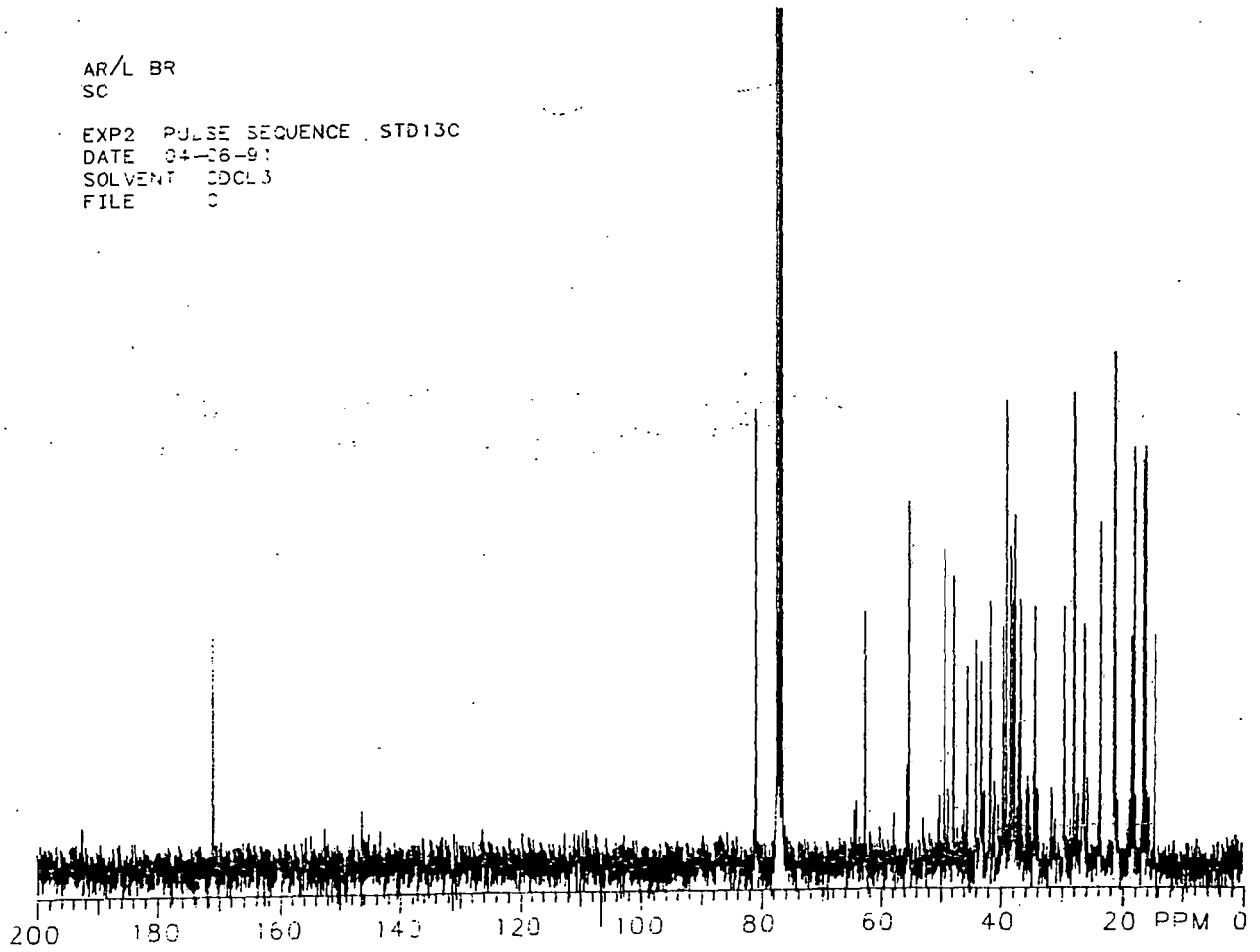


Fig. 9, ^{13}C NMR spectrum of 3β-acetyl 19α,29,30 tribromo Oleanane, 59.

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.

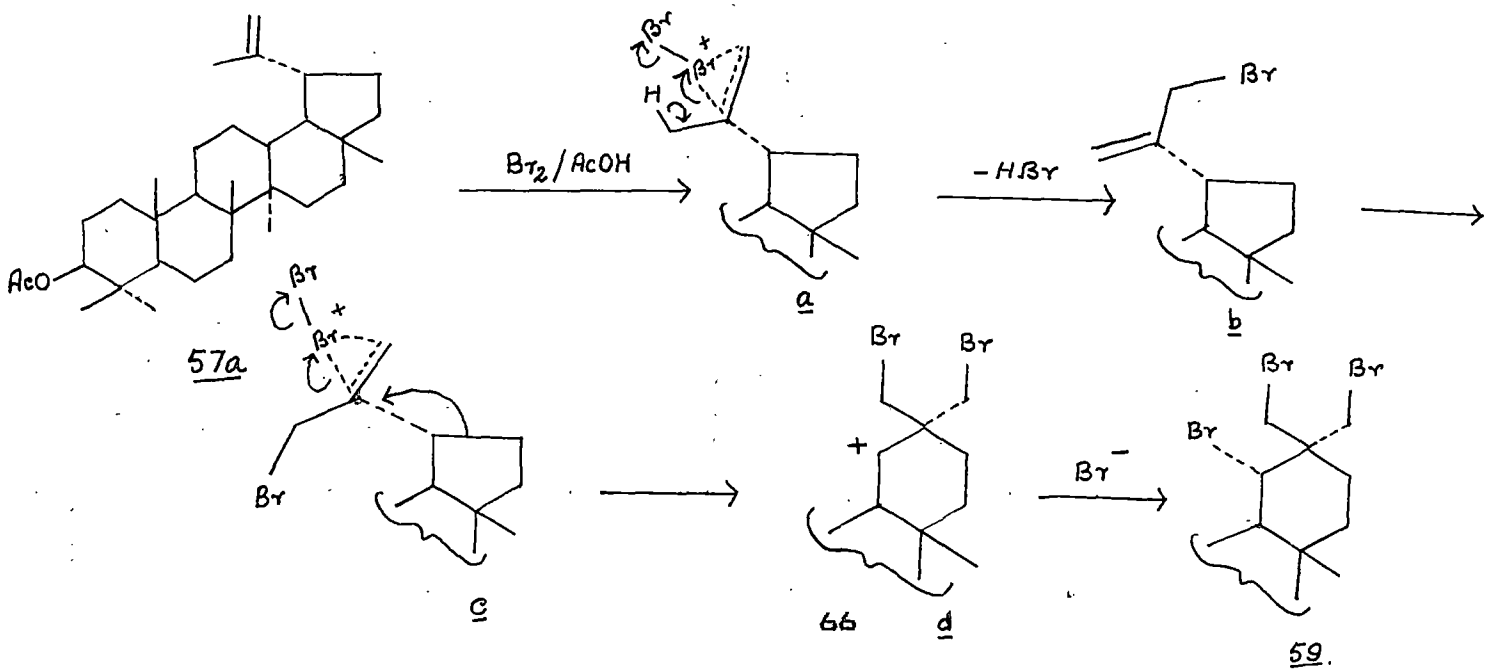
Assuming that the reaction with bromine in acetic acid on lupenyl acetate also proceed by almost the same mechanism the product-D may be assigned the structure **59**, which clearly explains the spectral data observed so far.

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.

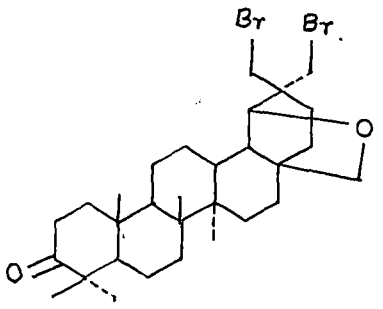
Characterisation of compound-E : Isolation of 3-keto olean 28-19-oxo-29,30-dibromide.

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.

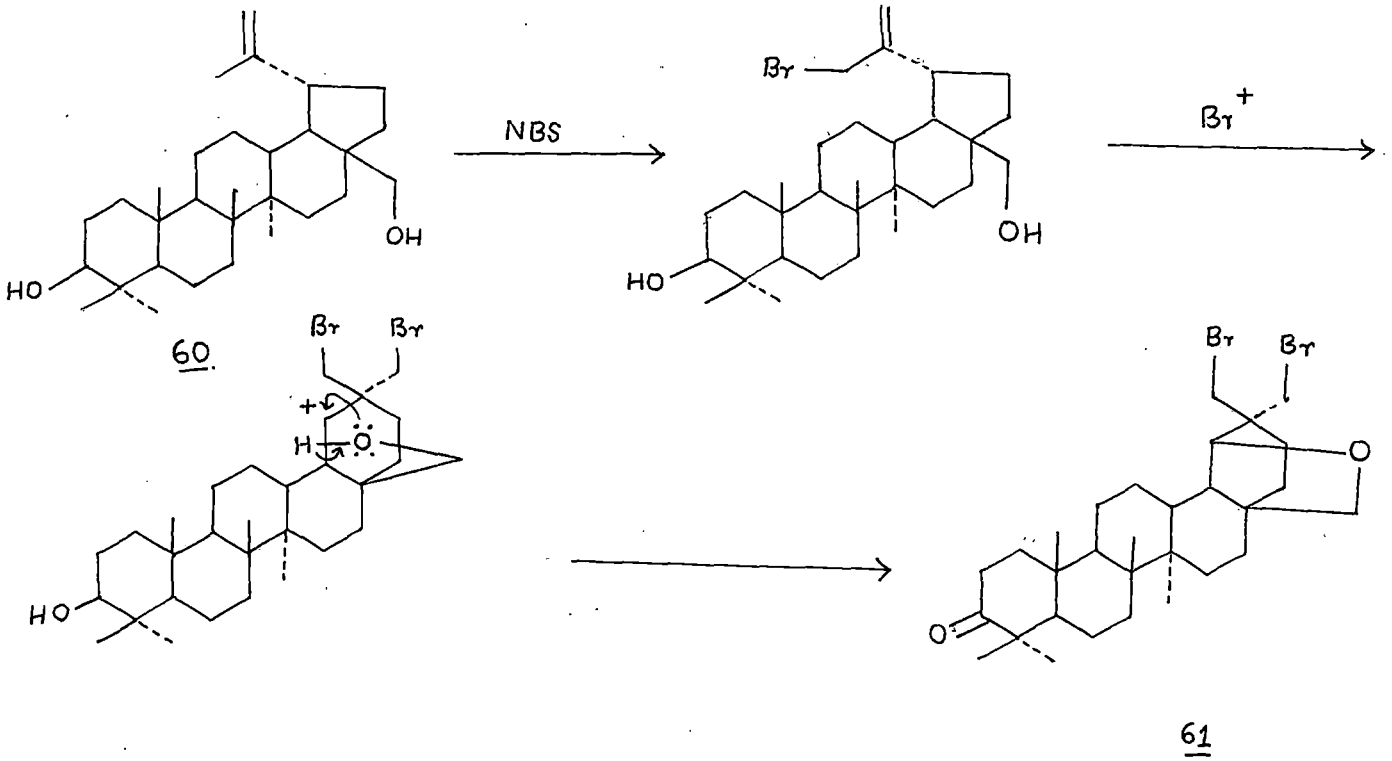
Hence compound-E was identified as 3-keto olean 28-19-oxo 29,30 dibromide 61 from the above spectral analysis.



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

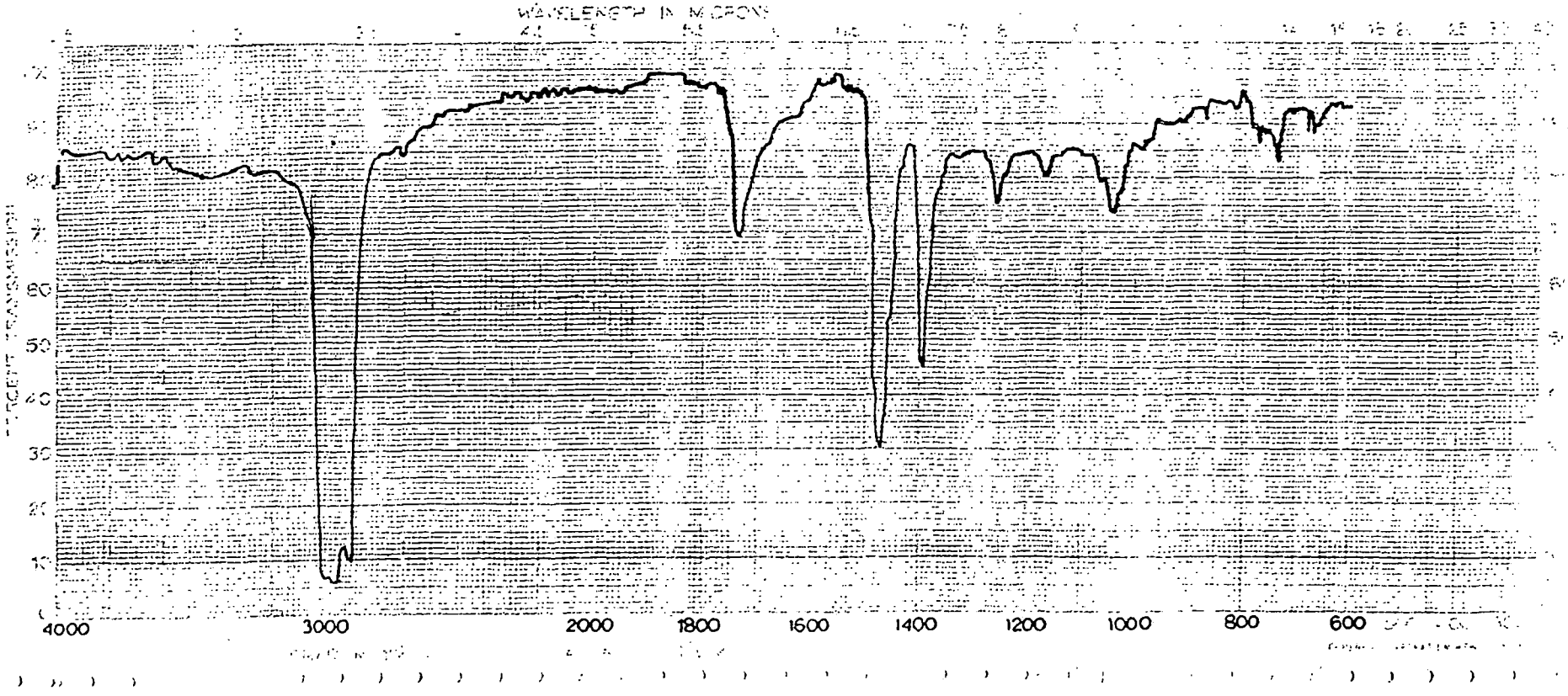


Fig. 10, IR spectrum of 3-keto Olean 28-19-oxo 29,30 dibromide, 61.

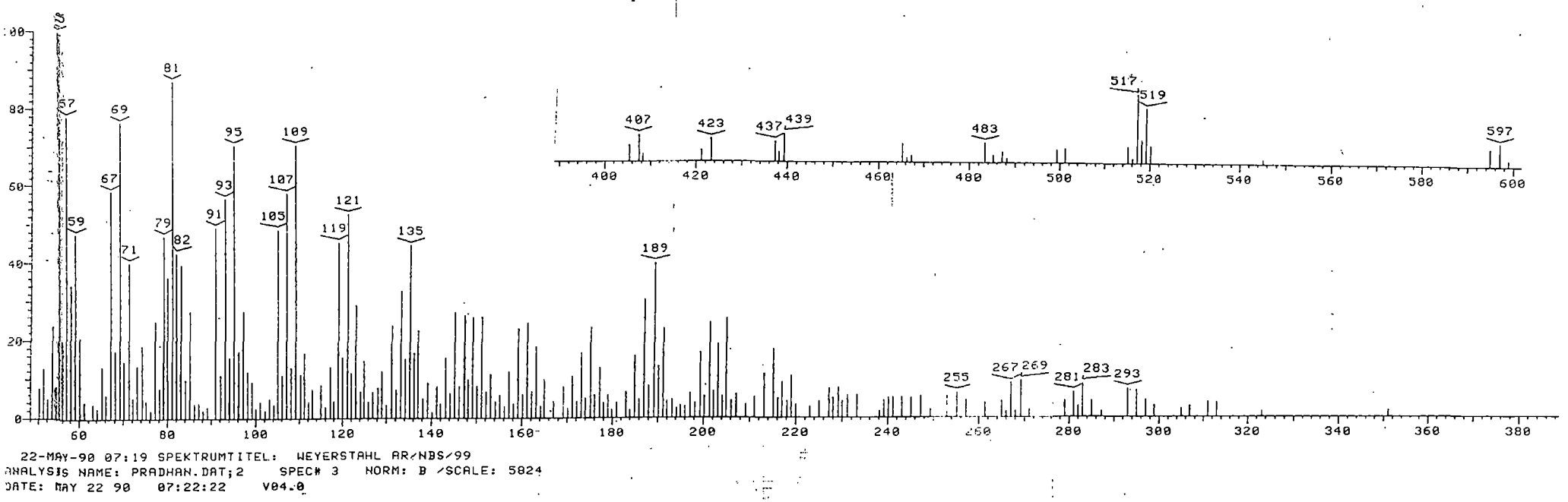


Fig. 11, Mass spectrum of 3-keto-Olean 28-19-oxo 29,30 dibromide, 61.

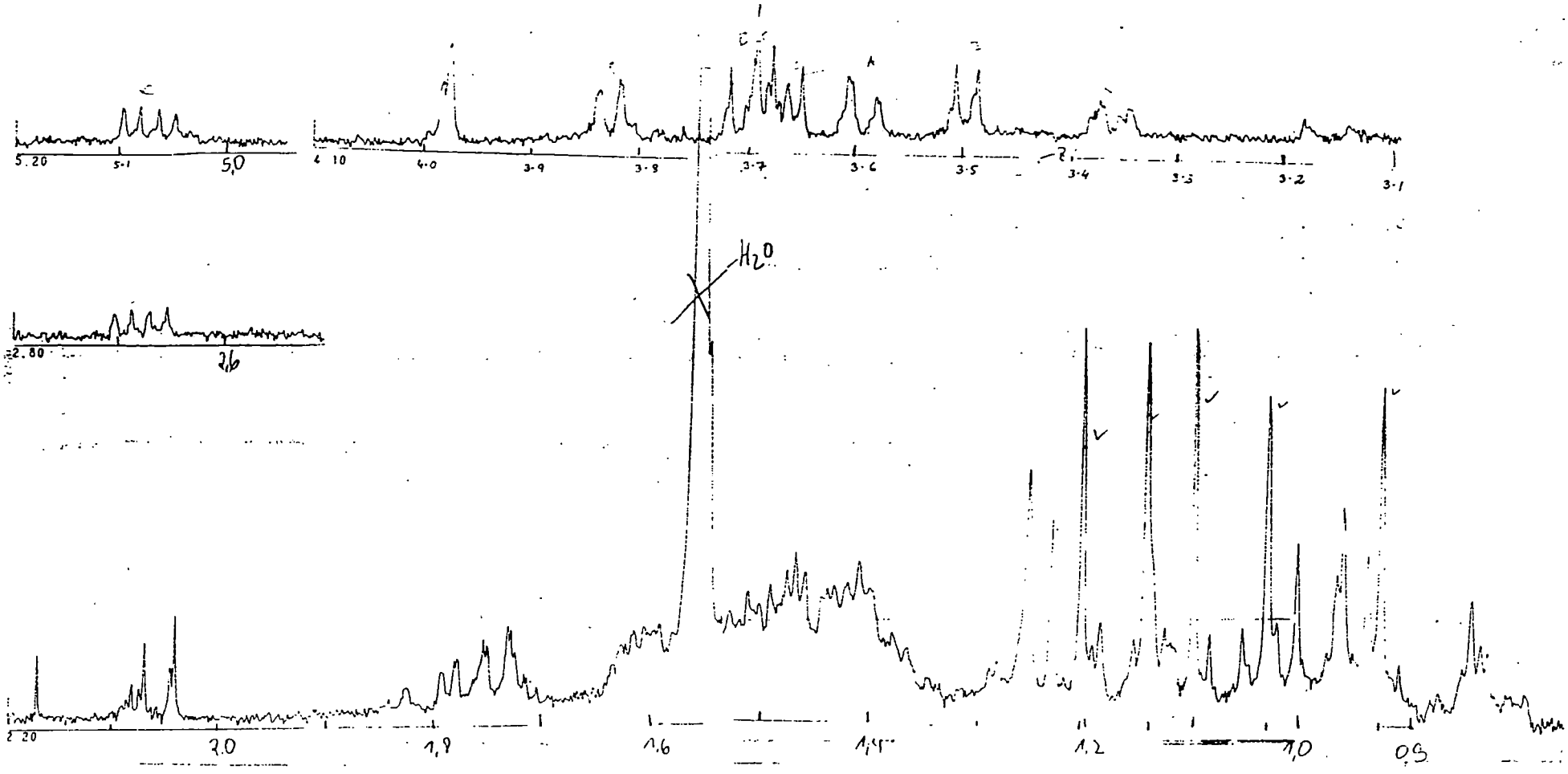


Fig. 12. ^{1}H NMR spectrum of 3-keto Olean 28-19-oxo 29,30 dibromide, 61.

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	"	

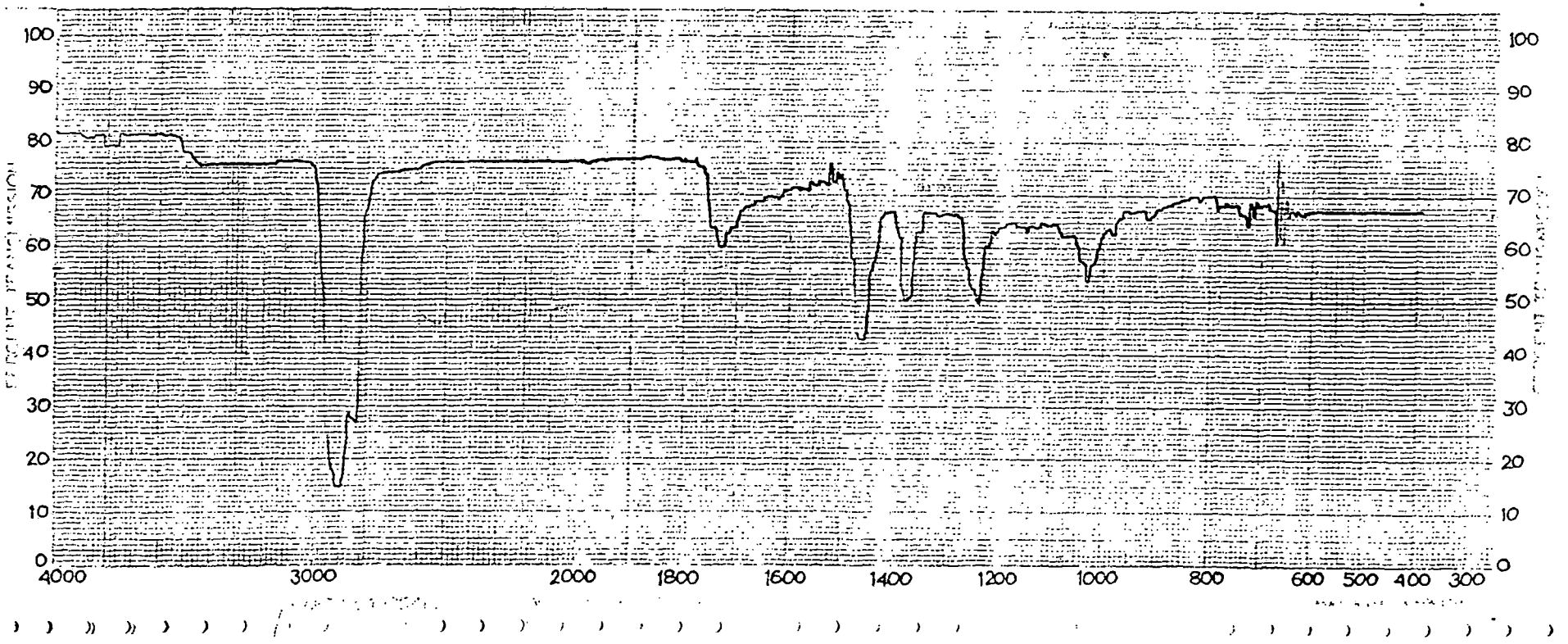


Fig. 13, IR spectrum of 30-bromo Lup-20(29)-ene 3β,28-diyl acetate, 63.

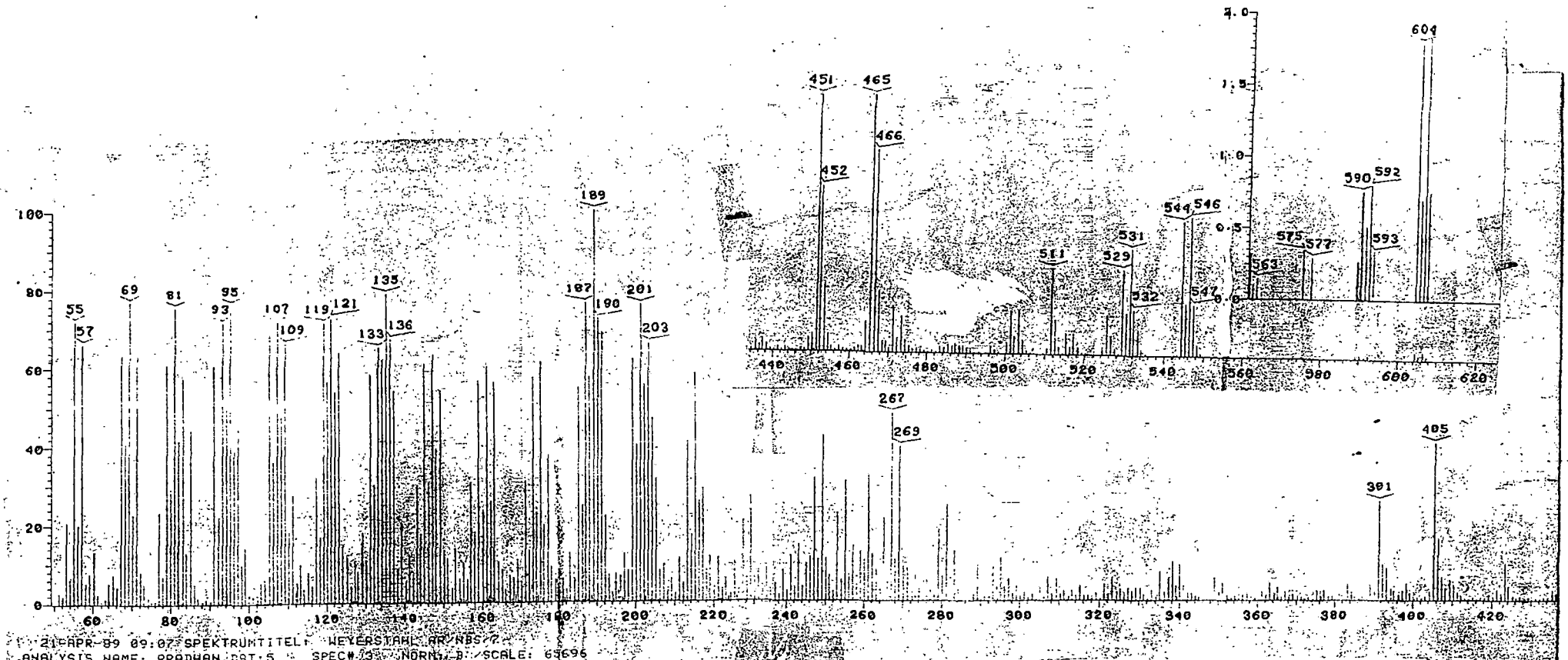


Fig. 14, Mass spectrum of 30-bromo Lup-20(29)-ene 3β,28-diyl acetate, 63.

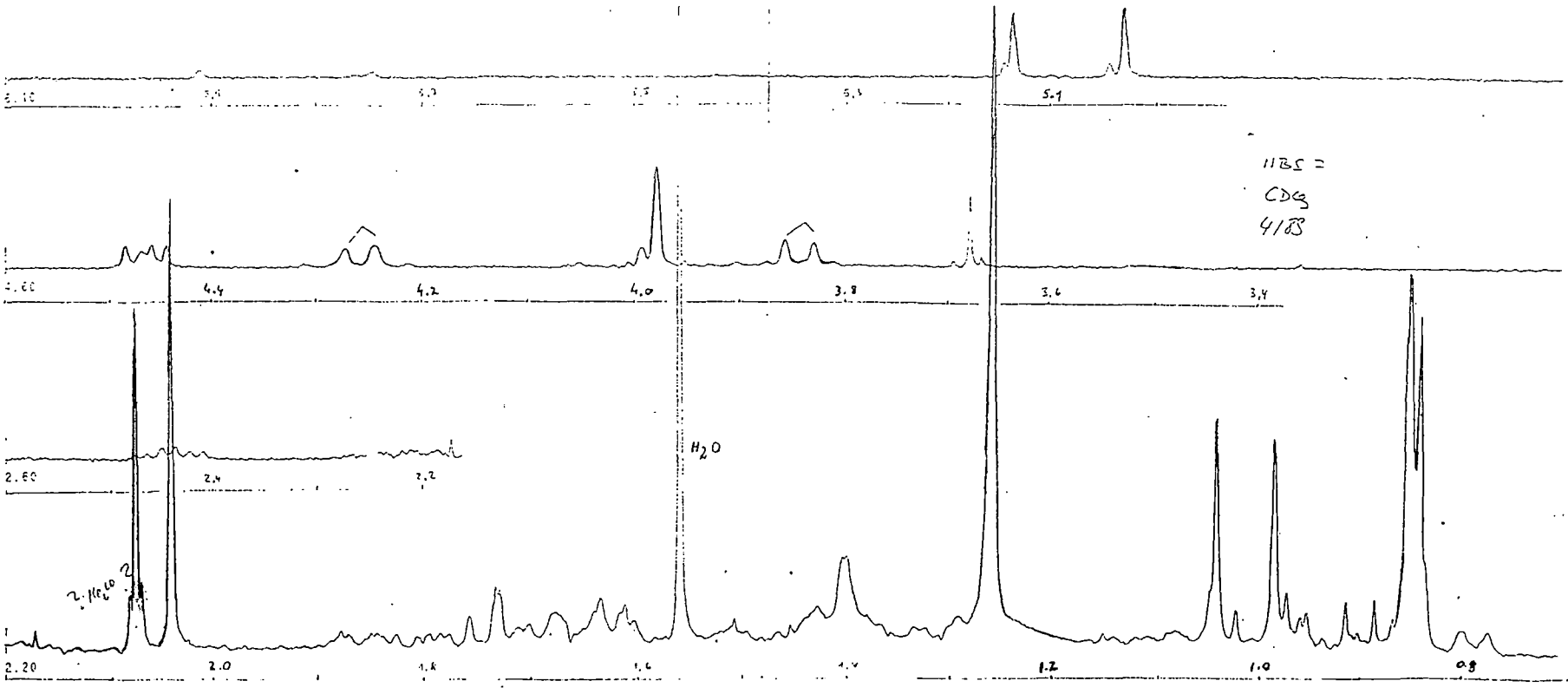
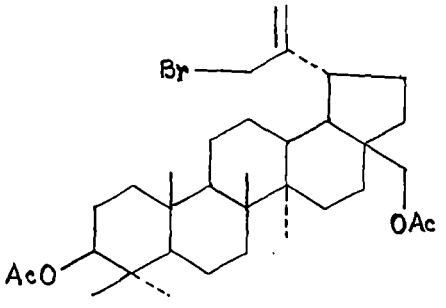


Fig. 15, ^{1}H NMR spectrum of 30 bromo Lup-20(29)-ene 3β,28-diyl acetate, 63.

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 :-

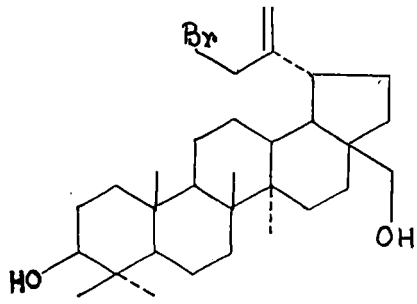
The compound G was crystallised from cloroform-methanol, *M.P.*202-3^{o}C; It gave yellow colouration with TNM showing the presence of double bond and responded to Beilstein test for halogen. IR spectrum (fig.16) showed broad absorption peak at 3390 cm^{-1} indicating the presence of hydroxy group while 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.

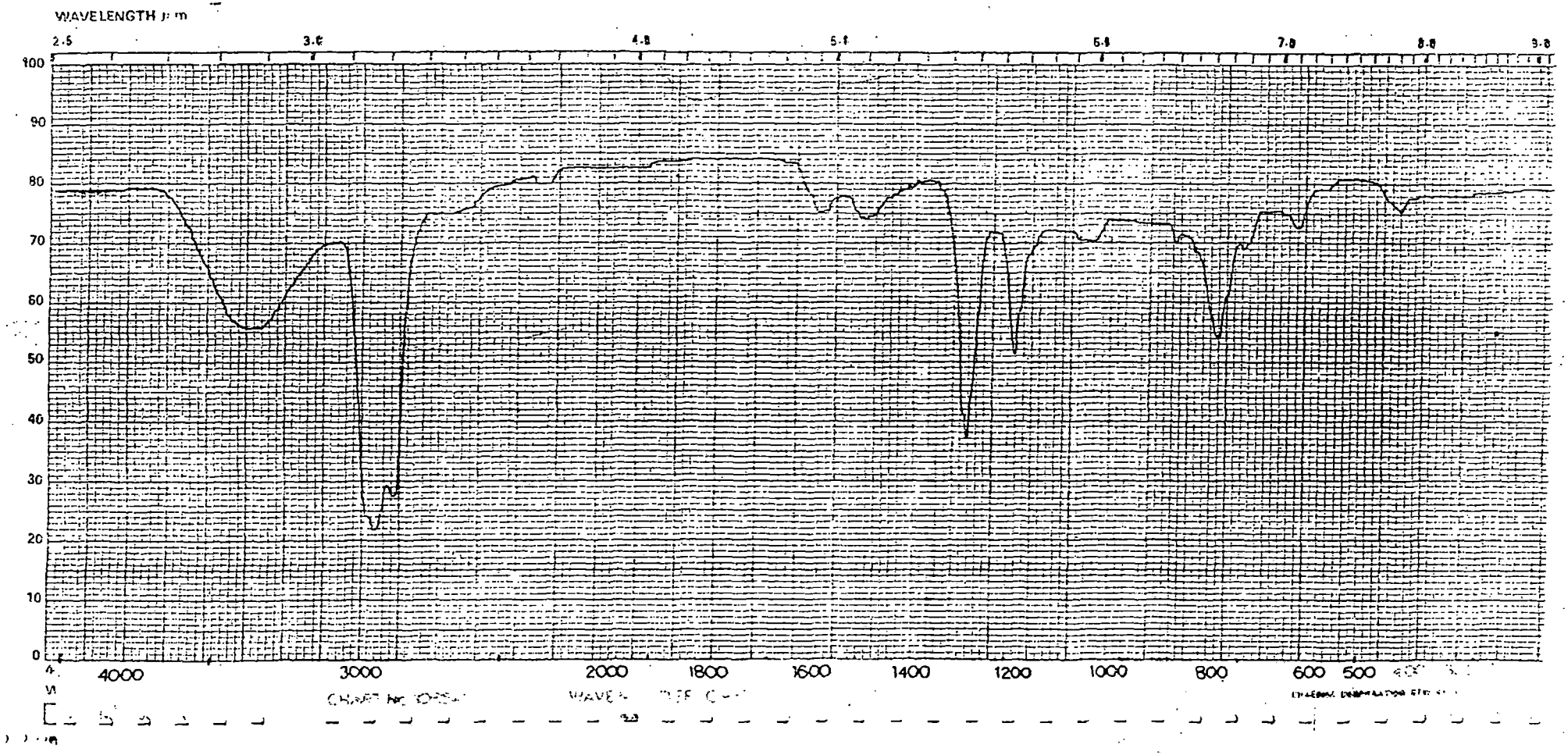


Fig. 16, IR spectrum of 30-bromo Lup-20(29)-ene 3β,28-diol, 64.

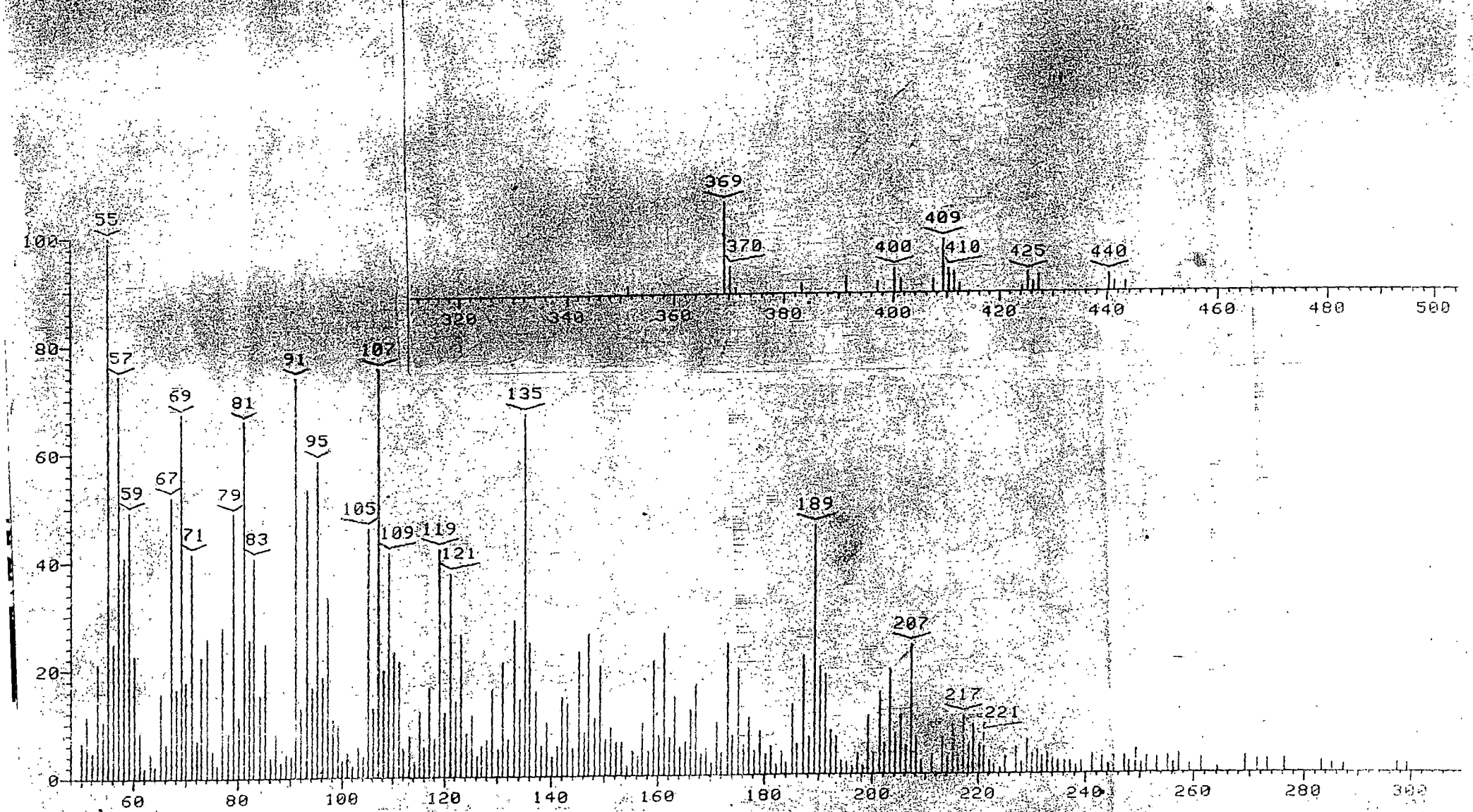


Fig. 17. Mass spectrum of 30-bromo Lup-20(29)-ene 3β,28-diol, 64.

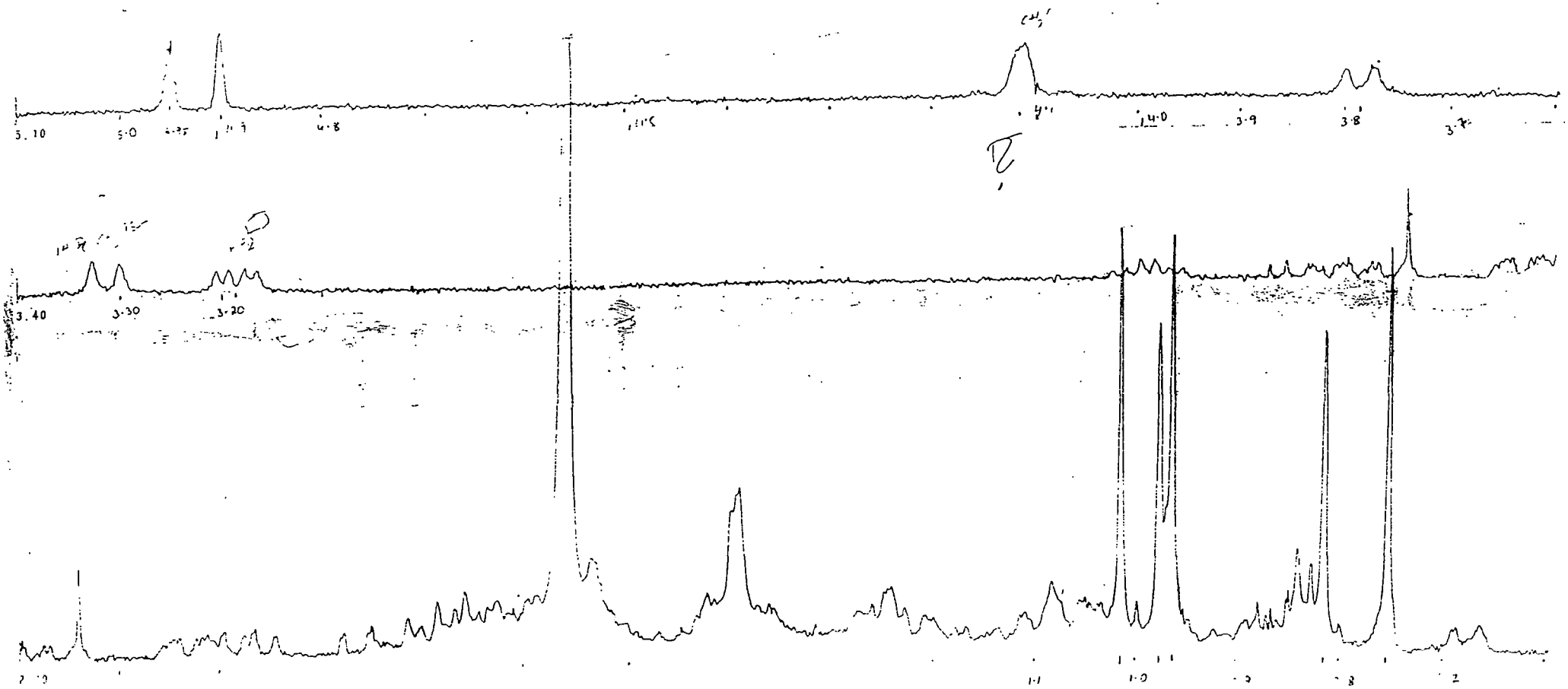


Fig. 18, ^{1}H NMR spectrum of 30-bromo Lup-20(29)-ene 3β,28-diol, 64.

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

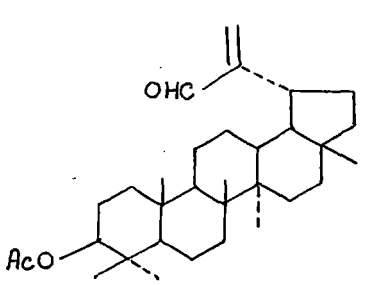
The compound lupan-20(29)-en-3,30-diyl acetate (prepared from lupenyl acetate, see Experimental) **67**, was dissolved in chloroform containing dimethyl sulfoxide and N-bromosuccinimide was added. The mixture was than kept in dark for 24 hours and the product thus obtained was chromatographed, which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

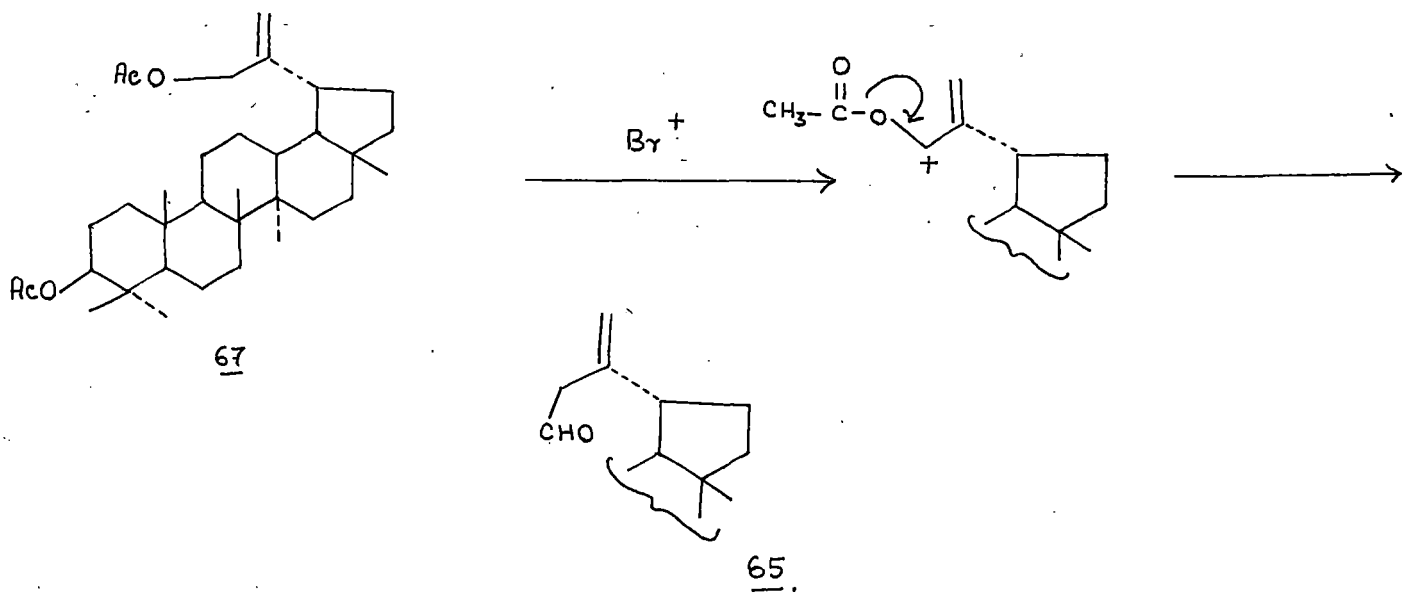


65

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.

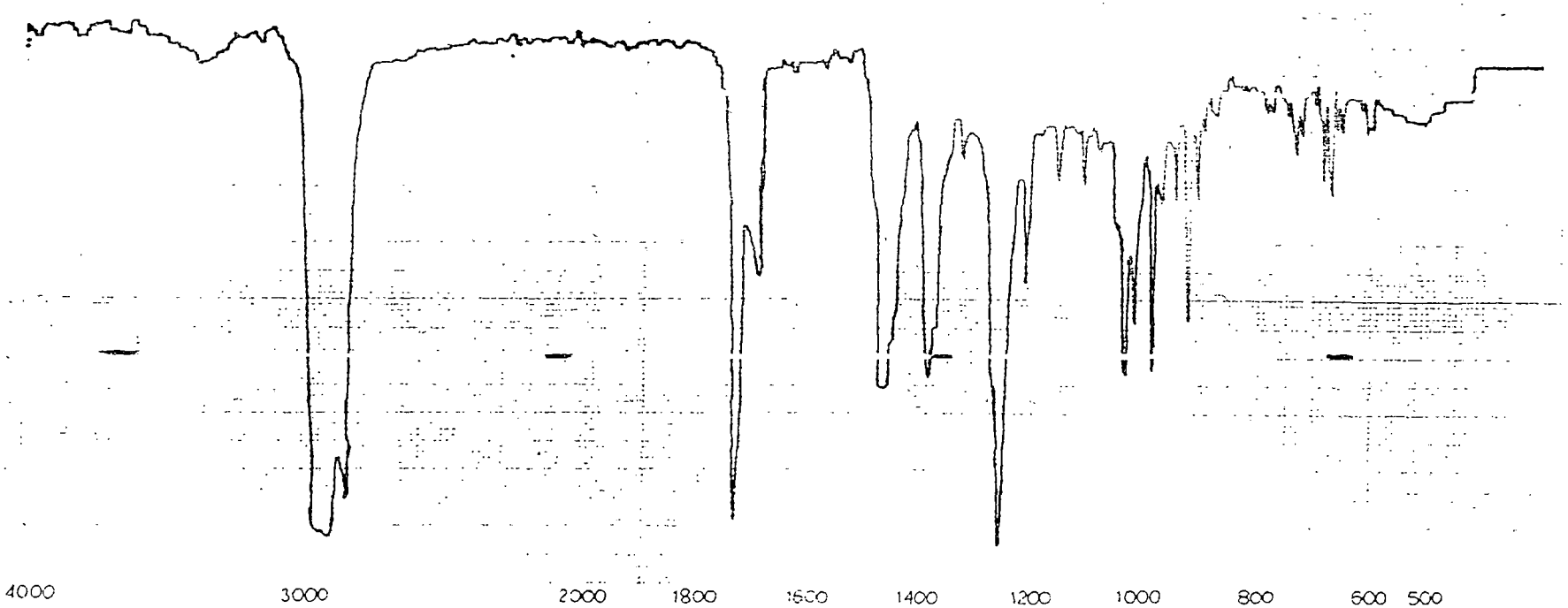


Fig. 19. IR spectrum of lupan 20(29)-en,30-al-3β-yl acetate,65.

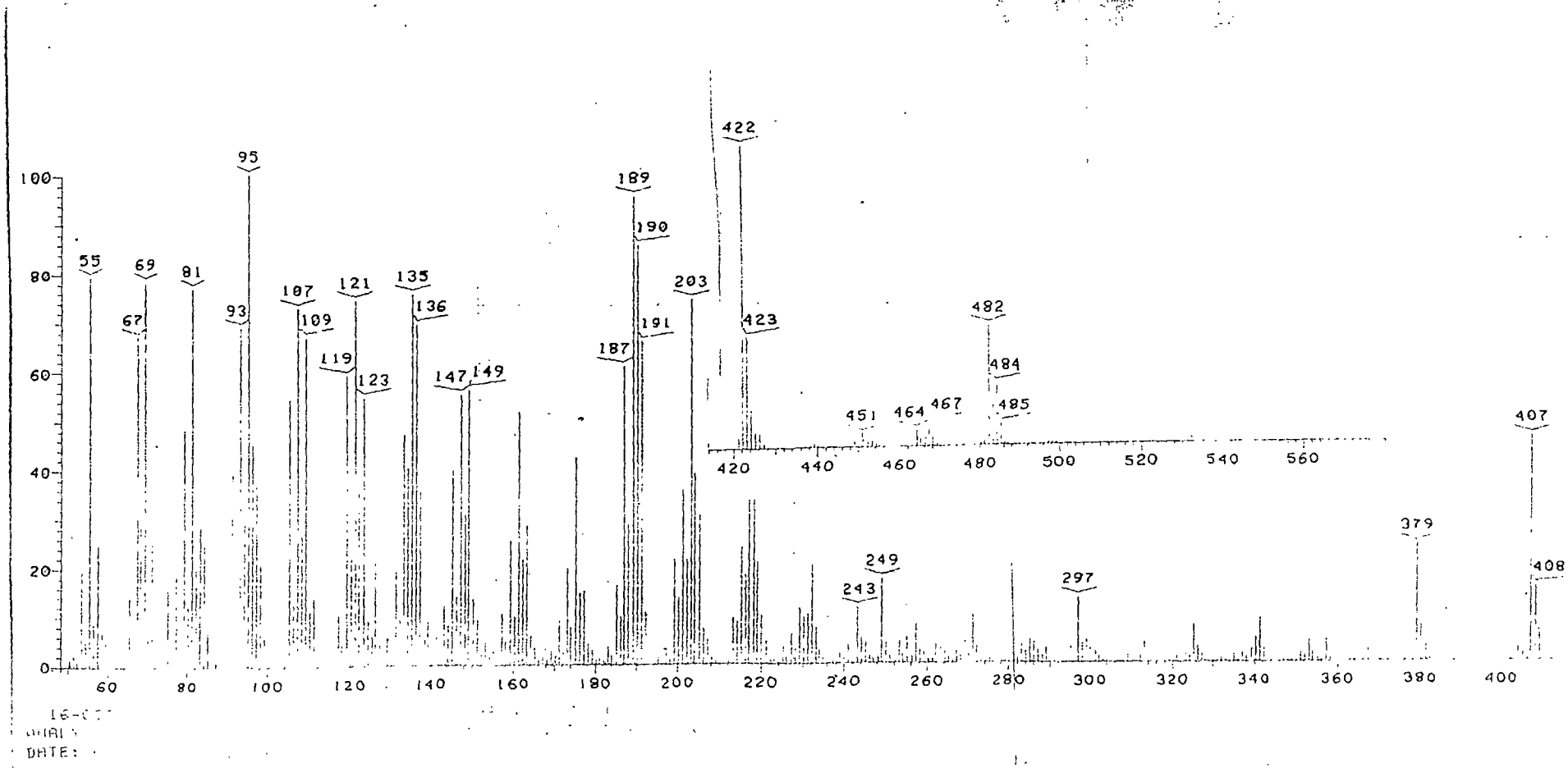


Fig. 20 Mass spectrum of lup 20(29)-en, 30-al, 3β-yl acetate, 65.

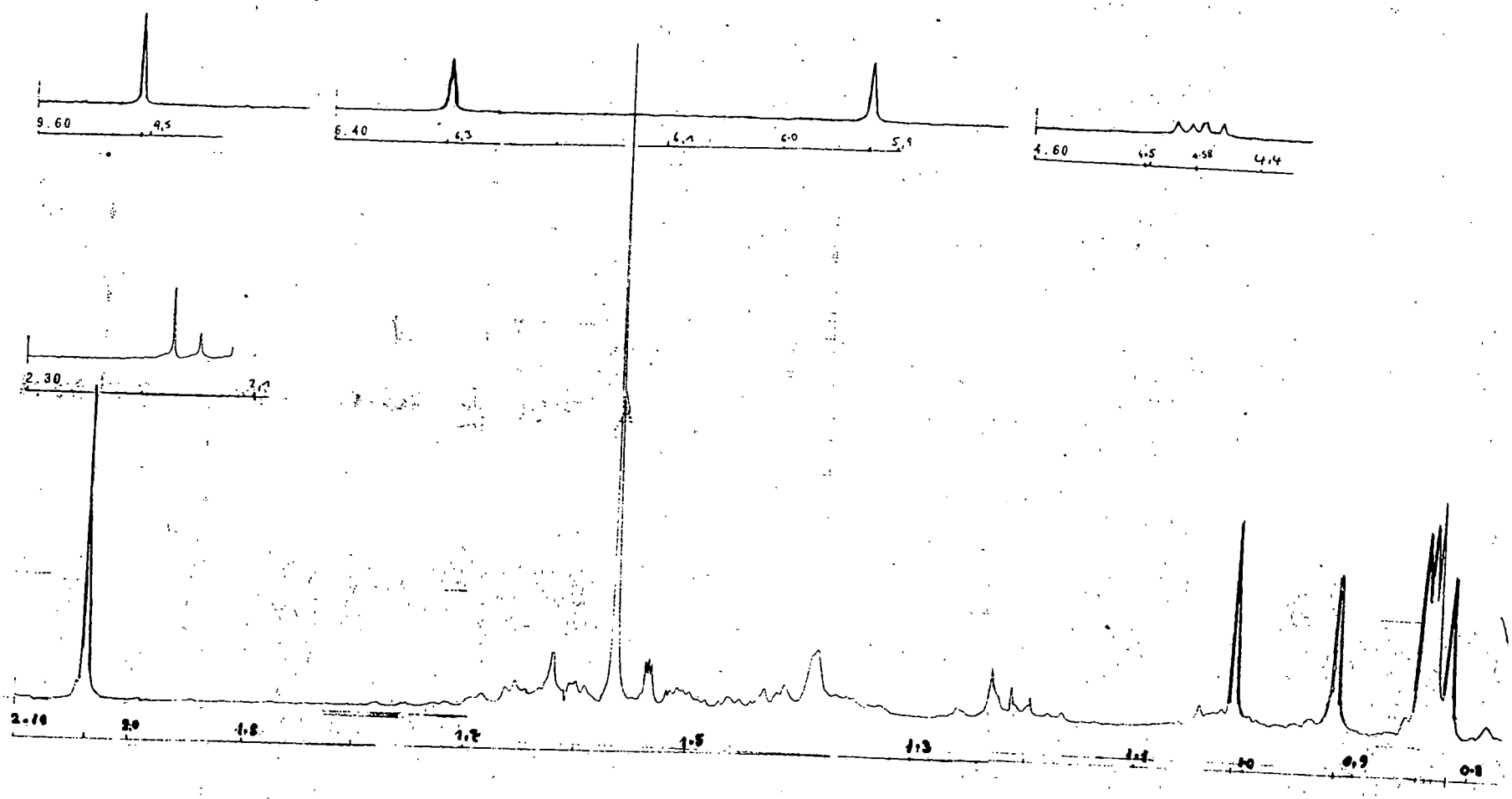


Fig. 21. ^{1}H NMR spectrum of lup-20(29)-en, 30-al, 3β-yl acetate, 65.

Friedel-3(4)-ene **54** was prepared from friedelin by the same method as discussed in experimental section of part -I in this thesis.

OXIDATION OF FRIEDEL-3(4)-ENE **54** *BY N-BROMOSUCCINIMIDE* (NBS) *IN DIMETHYL SULFOXIDE* (DMSO).

1.0 g of friedel-3(4)-ene **54** was dissolved in 10 ml of $CHCl_3$ and 100 ml of DMSO was added. Then 1.0 g of NBS was added in small lots of 0.1 g each and the mixture was kept in dark for 24 hours. It was then diluted with $CHCl_3$, taken in a separating funnel and was washed with water till there was no smell of DMSO. It was then dried over anhydrous Na_2SO_4 and the solvent was distilled off yielding a gummy solid which showed two distinct spots in tlc plates.

The gummy mass was dissolved in minimum volume of benzene and subjected to column chromatography the result of which are given in tabular form below :-

TABLE-I

Eluent	Fraction of 50 ml each.	Residue on distillation.
1. petrol	1-4	solid, (0.2 g)
2. petrol-benzene (4:1)	5-10	solid, (0.4 g)

further elution did not yield any more solid.

The fractions 1-4 were crystallised from $CHCl_3$-MeOH, *M.P.* 200-1°C; showed positive Beilstein test for halogen and gave yellow colouration with TNM. It was identified as 3α-bromo-Olean $\Delta^{13(18)}$-ene **55** from spectral analysis.

ANALYSIS REPORT.

Found :	C 73.0 ; H 9.7%
Calculated for $C_{30}H_{49}Br$:	C 73.6 ;: H 10.02%

Mass : m/e	490 (M_1^+,Br^{79}),488 (M_2^+,Br^{77}) 475, 473, 410, 408, 395, 274, 257, 218, 205, 109, 95(100). fig.1.
^1H NMR : ($CDCl_3$) (δ in ppm)	0.79,0.81,0.83,0.84,0.86, 0.94 and 1.08(bs) (6s,3H each & one 6H,8X t-Me) 1.81 (td,1H,J=3 & 13 Hz, C_9-αH) 5.16 (bs, $W_{1/2}$=8 Hz, C_3-βH). fig.2.

The fractions 5-10 were combined and crystallised from $CHCl_3$-MeOH, *M.P.*229-30^oC; did not respond to Beilstein test for halogen but gave yellow colour with TNM. It was identified as 3β-hydroxy olean $\Delta^{12(13)}$-ene **56** from spectral datas.

ANALYSIS REPORT.

Found :	C 83.9 ; H 11.2%
Calculated for $C_{30}H_{50}O$:	C 84.5 ; H 11.73%

IR (Nujol) : ν_{max}	3380 cm^{-1} (-OH) fig.3.
Mass : m/e	426 (M^+), 411, 408, 395, 393, 255, 229, 205, 173, 145, 125, 123, 95(100). fig.4.

^{1}H NMR : ($CDCl_3$)	0.79,0.81,0.82,0.87,0.94,
(δ in ppm)	0.99 and 1.06(bs)
	(6s,3H each & one 6H,8X t-Me)
	4.08 (bs,1H, C_3-βH)
	5.53 (t,1H, C_{12}-H)

fig.5.

BROMINATION OF LUPENYL ACETATE **57a** *BY BROMINE IN ACETIC ACID*

1.0 g. of lupenyl acetate **57a** was dissolved in 100 ml of acetic acid and allowed to cool at -5^oC with freezing mixture. Than 8 ml of bromine was added dropwise with constant shaking. The mixture was than poured in ice cold water, extracted with ether, washed with water repeatedly, dried with anhydrous sodium sulphate and finally the solvent ether was distilled off yielding a yellowish solid mass. It was dissolved in minimum benzene and chromatographed over silica gel column. On elution with petrol a crystalline white solid compound (0.3 g) was obtained. It was recrystallised from $CHCl_3$-MeOH, M.P.225-6^oC, identified as 3β-acetyl oleanan 19α,29,30 tribromide **59**.

BROMINATION OF LUPENYL ACETATE **57a** *WITH* NBS *IN CARBON TETRACHLORIDE.*

1.0 g of lupenyl acetate **57a**, *M.P.*212-3^oC, was dissolved in 100 ml of carbon tetrachloride and refluxed over waterbath with 1.0 g of NBS for 4 hours. It was than kept overnight and unreacted NBS was filtered, solvent was distilled off and the product obtained was chromatographed which on elution with petrol-benzene (4:1) gave white crystals, recrystallised from chloroform-methanol, M.P. 225-6^oC, gave yellow colouration with TNM and responded to Beilstein test for halogen; IR : 1725, 1255 (-OCOCH_3), 3015, 1640 and 880 cm^{-1} (C=CH_2); identified as 30-bromo lupenyl acetate **58**, *M.P.*235-6^oC ; [Lit.*M.P.* 235-6^oC] by comparison with authentic sample (prepared earlier).

ANALYSIS REPORT

Found :	C 54.02 ;	H 7.10
Calculated for $C_{32}H_{51}O_2Br_3$:-	C 54.08 ;	H 7.18

IR (Nujol) : ν_{max}	1690 and 1255 cm^{-1} ($-OCOCH_3$)
	fig.6
Mass : m/e	710 (M^+),708,706,648,646,626 568,566,633,487,466,376,362 267,231,189,175,135,95,82, 80 (100).
	fig.7
^1H NMR : ($CDCl_3$) (δ in ppm)	0.84,0.85,0.86,0.94,0.95,1.06 (6s,18H.6 X t-CH_3)
	2.05 (s,3H,$-OCOCH_3$)
	3.5-3.9 (AB_q, J=10 Hz,$-CH_2Br$)
	3.8-4.6 (AB_q,J=11.5 Hz,$-CH_2Br$)
	4.24 (d,1H, C_{19}-βH)
	4.48 (m,1H, C_3-αH)
	fig.8
^{13}C NMR :	fig.9

Betulinic acid was isolated and esterified by same method as discussed in the experimental section of part-I of this thesis.

LAH REDUCTION OF METHYL BETULINATE : PREPARATION OF LUPAN 20(29)-EN-3β,28-DIOL **60**.

3.0 g of methyl betulinate was dissolved in 400 ml dry ether and 8.0 g of LAH was added cautiously to the cold ethereal solution. The mixture was than refluxed for 6 hours over heating mentle. It was than cooled to room temperature and excess LAH was destroyed with saturated solution of sodium sulfate when a white inorganic salt coagulated. The supernatant solution was decanted and the residue was washed with fresh chloroform. The decanted and chloroform solution was washed with water, dried and the solvent was distilled off. The solid obtained (2.4 g) was crystallised from $CHCl_3$-MeOH mixture to furnish white crystals of lupan 20(29)-ene 3β,28-diol **60** (Betulin), *M.P.* 258°C, $[\alpha]_D$=+ 17°, IR : 3350, 3370 (-OH) and 890 cm^{-1} (C=CH_2),TNM test +ve; identical with authentic sample (*M.M.P.* and CO-tlc)

Found :	C 81.25% ; H 10.95%	
Calculated for $C_{30}H_{50}O_2$:	C 81.45% ; H 11.31%	

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

1.0 g of lupan 20(29)-en-3β,28-diol **60** was dissolved in 7-8 ml of $CHCl_3$ and 35 ml of DMSO was added. Than 1.0 g of NBS was added in small lots of 0.1 g each with constant shaking and it was kept in dark for 24 hours. The mixture was then poured in ice cold water when a solid material separated out which was extracted with excess $CHCl_3$. The $CHCl_3$ layer was washed with water repeatedly till free from DMSO, dried over anhydrous sodium sulfate and finally the solvent was distilled off to furnish a gummy mass (0.85 g). Tlc of the latter showed a single spot indicating the presence of at least one new product. The gummy mass was dissolved in minimum volume of benzene and chromatographed over silica gel column.

Elution with petrol furnished a solid mass, designated as compound E, *M.P.*232-3°*C*; identified as 3-keto-oleanan-28-19-oxo-29,30-dibromide **61**.

ANALYSIS REPORT.

Found :	C 60.0% ; H 7.4%
Calculated for $C_{30}H_{46}O_2Br_2$:	C 60.1% ; H 7.6%

IR (Nujol) : ν_{max} 1720 cm^{-1} (C=O)

fig **10**

Mass : m/e 599 (M^+),519, 517, 488, 439, 423, 407, 293, 283, 267, 189, 107, 95, 81, 55(100)

fig.**11**

^1H NMR : ($CDCl_3$) (δ in ppm)

0.93, 1.03, 1.10, 1.14 and 1.21 (5s,15H, t-CH_3)
2.68 (m,2H,-$COCH_3$)
3.69 (AB_q, J=5 Hz, -C_{28}-H_2-)
3.50-3.71 (AB_q, 10 Hz,-CH_2Br)
3.59-3.82 (AB_q, 10 Hz,-CH_2Br)
3.98 (d,J=3 Hz, -C_{19}-H)

fig.**12**

ACETYLATION OF BETULIN,60 ; PREPARATION OF BETULIN DIACETATE,62.

1.5 g of betulin, **60** was dissolved in 10 ml pyridine and 15 ml of acetic anhydride was added. The mixture was heated over water bath for 6 hours. After usual workup and chromatography, a solid material was obtained with eluent petrol-benzene mixture (4:1) which was crystallised from $CHCl_3$-MeOH to afford white crystals of betulin diacetate, *M.P.* 222-3°C, $[\alpha]_D$= +21°; IR : 1740,1250 ($-O-COCH_3$) and 1650,900 cm^{-1} ($C=CH_2$).

Found :	C	77.36%	;	H	10.06%
Calculated for $C_{34}H_{54}O_4$:	C	77.56%	;	H	10.26%

OXIDATION OF BETULIN DIACETATE 62 BY NBS IN DMSO

0.5 g of betulin diacetate **62** was dissolved in minimum $CHCl_3$ containing 25 ml of DMSO. Then 0.75 g of NBS was added in small lots and the mixture was kept in dark for 24 hours. On usual workup, the gummy product obtained was dissolved in minimum volume of benzene and chromatographed over silica gel column. The solvent used are shown in table below :-

TABLE-II.

	Eluent	Fraction of 50 ml each.	Residue on distilation.
1.	Petrol	1-4	nil
2.	petrol-benzene (4:1)	5-8	nil
3.	petrol-benzene (3:2)	9-11	nil
4.	petrol-benzene (2:3)	12-15	solid,(0.2 g)
5.	petrol-benzene (1:4)	16-18	nil
6.	benzene	19-23	solid,(0.2 g)

Further elution did not afford any more solid.

Fractions 12-15 were crystallised together from $CHCl_3$-MeOH; *M.P.* 169-70°C, identified as 30-bromo lup-20(29)-en-3β,28-diyl acetate **63.**

ANALYSIS REPORT

Found :	C 67.3 ;	H 8.90%
Calculated for $C_{34}H_{54}O_4Br$:	C 67.33 ;	H 8.91%

IR (Nujol) : ν_{max} 1730 and 1240 cm^{-1} ($-OCOCH_3$)

fig.**13**

Mass : m/e 606(M^+),604,593,592, 577,546,531,511,466, 465,451,405,267,201, 189(100)

fig.**14**

^{1}H NMR : ($CDCl_3$) (δ in ppm.)

0.83,0.85,0.98,1.05 and 1.26 (5s,15H,5 X t-CH_3)

2.03 and 2.07 (2s,6H,2 X $-COCH_3$)

3.91 (s,2H,$-CH_2OAc$)

3.84 and 4.26 (dd,2H,$-CH_2Br$)

5.03 and 5.12 (2s,2H, $C=CH_2$)

fig. **15**

Fractions 19-23 were crystallised together from $CHCl_3$-MeOH, *M.P.* 202-3°C, identified as 30-bromo lup-20(29)-en$\not$-3β,28-diol **64.**

ANALYSIS REPORT

Found :	C 68.8 ;	H 9.50%
Calculated for $C_{30}H_{50}O_2Br$:	C 68.97 ;	H 9.57%

IR (Nujol) : ν_{max}	3390 cm^{-1} (broad) (-OH)

fig.**16**

Mass : m/e	442,440,425,409,369, 207,189,135,107,91, 55(100)

fig.**17**

^{1}H NMR : ($CDCl_3$) (δ in ppm)	0.76,0.82,0.96,0.98 and 1.02 (5s,15H,5 X t-CH_3)
	3.19 (m,1H, C_3-αH)
	3.15 and 3.78 (dd, J=10 and 10 Hz,-CH_2Br)
	4.12 (bs,2H,-CH_2OH)
	4.90 and 4.95 (2s,2H,-CH_2=C)

fig.**18**

ACETYLATION OF LUPEOL : PREPARATION OF LUPENYL ACETATE **57a**.

1.0 g of lupeol **57** was dissolved in 15 ml of pyridine and 20 ml acetic anhydride was added. The mixture was heated over waterbath for 4 hours and poured in ice cold water when a white solid of lupenyl acetate **57a** separated out. It was filtered through suction, washed with water and dried in air. *M.P.* 212-13°C, [lit. *M.P.*213-14°C]

OXIDATION OF LUPENYL ACETATE **57a** *IN ACETIC ACID WITH* SeO_2 *: PREPARATION OF LUPAN 20(29)-EN-30-AL,3β-YL ACETATE* **65**

1.0 g of lupenyl acetate was dissolved in 150 ml of acetic acid and refluxed with 1.0 g of SeO_2 over heating mentle for 1 hour. Then it was poured in ice cold water when solid crystals of lupan 20(29)-en-30-al-3β-yl acetate **65** separated out. It was filtered, washed with water till neutral and dried,*M.P.* 224-5°C, [lit. *M.P.* 224-25°C] IR : 1730,1700 and 1255 cm^{-1}, gave yellow colouration with TNM.

REDUCTION OF LUPAN 20(29)-EN-30-AL-3β-YL ACETATE **65** *WITH LAH : PREPARATION OF LUPAN 20(29)-EN-3β,30-DIOL* **66**.

1.0 g of lupan 30-al- 3β-yl acetate **65** was dissolved in dry ether and 1.5 g of LAH was added. The mixture was then refluxed for 5 hours over heating mentle and allowed to cool at room temperature. After usual workup, the product was extracted with ether, washed, with water, dried and the ether was distilled off giving a white solid (0.7 g). It was crystallised from $CHCl_3$-MeOH, *M.P.* 231-2°C, produced yellow colouration with TNM; IR : 3400 and 3320 cm^{-1} (-OH) identified as lupan 20(29)-en-3β,30-diol **66**.

ACETYLATION OF LUPAN 20(29)-EN-3β,30-DIOL **66** *: ISOLATION OF LUPAN-20(29)-EN-3β,30- DIYL-ACETATE* **67**

0.6 g of lupan 20(29)-en,3β,30-diol **66** was heated over waterbath with of 10 ml pyridine and 15 ml of acetic anhydride. It was than poured in ice cold water when white crystals of lupan 20(29)-ene-3β,30-diyl acetate **67** was separated out. It was filtered, washed with water and dried in air, *M.P.* 253-4°C, IR : 1750,1740,1250 and 1230 cm^{-1}.

OXIDATION OF LUPAN-20(29)-EN-3β,30-DIYL ACETATE **67** *WITH NBS IN DMSO :-*

0.5 g of lupan-20(29)-en-3β,30-diyl actate **67** was dissolved in minimum volume of $CHCl_3$ followed by 20 ml of DMSO and than 0.75 g of NBS was added. The mixture was than kept in dark for 24 hours and than usual workup gave a gummy yellow product which was chromatographed in silica gel column.

TABLE-III

Eluent	Fraction of 50 ml each	Residue on distillation.
1. petrol	1-3	nil
2. petrol-benzene	4-6	nil

(4:1)		
3. petrol-benzene (3:2)	7-10	nil
4. Petrol-benzene (2:3)	11-13	nil
5. benzene	14-18	solid, (0.35 g)

The fractions 14-18 were crystallised from $CHCl_3$-MeOH, *M.P.* 224-5^{o}C; TNM test positive, identified as lupan 20(29)-en-30-al,3β-yl acetate **65**.

ANALYSIS REPORT.

Found :	C 78.9% ; H 10.3%
Calculated for $C_{32}H_{50}O_3$:	C 79.6 ; H 10.37

IR (Nujol) : ν_{max} 1730, 1700 and 1255 cm^{-1} (-CHO, $-COCH_3$)
fig.**19**

Mass : m/e 482 (M^+),467,422,407,379, 297,249,203,189,149,135, 121,107 and 95 (100).
fig.**20**

^1H NMR : ($CDCl_3$) (δ in ppm)
0.82, 0.83, 0.84, 0.85 0.92 and 1.01 (6s,18H, 6X t-CH_3)
2.04 (s, 3H, $-COCH_3$)
5.93 and 6.31 (2s,2H, C=CH_2)
9.51 (s,1H, -CHO at C-30).
fig.**21**

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PART-III

OXIDATION OF PENTACYCLIC TRITERPENOID KETONE, LACTONE AND ESTER WITH META CHLOROPERBENZOIC ACID IN CHLOROFORM.

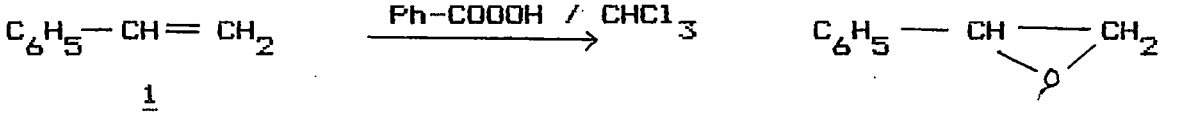
CHAPTER-I

A BRIEF REVIEW OF OXIDATIVE REACTIONS BY PER-ACIDS AND PEROXIDES.

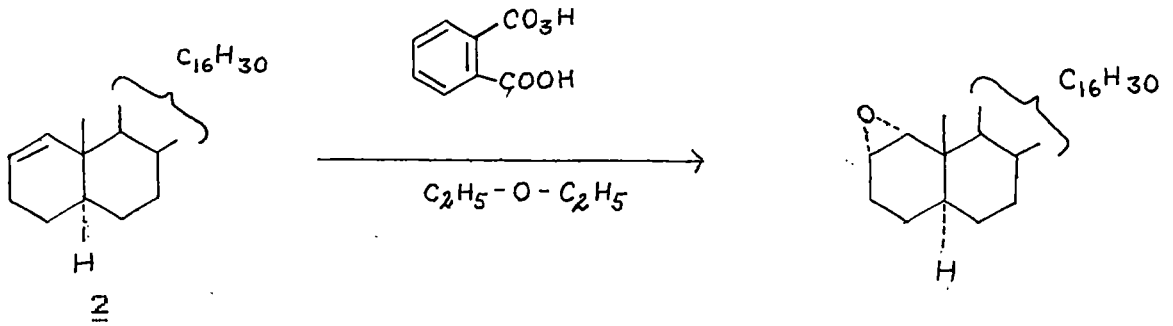
Peracids have been used most extensively for the selective oxidations of carbon-carbon double bonds,conversion of ketones to esters and recently functionalisation of unactivated carbon atoms. Among the peracids, commonly used are performic acid, perchloric acid, per-acetic acid,hydrogen peroxide, perbenzoic acid, benzoyl peroxide,meta-chloro perbenzoic acid (mCPBA), trifluoro per acetic acid and mono perphthalic acid. A few of them are prepared by the actions of hydrogen peroxide on their corresponding acid and the resulting reaction mixture is used as peracid. A short discussion is given below:

OXIDATION OF CARBON-CARBON DOUBLE BOND.

Olefins[1,2]. 1, 2 are converted to epoxides by peracids in good yield.

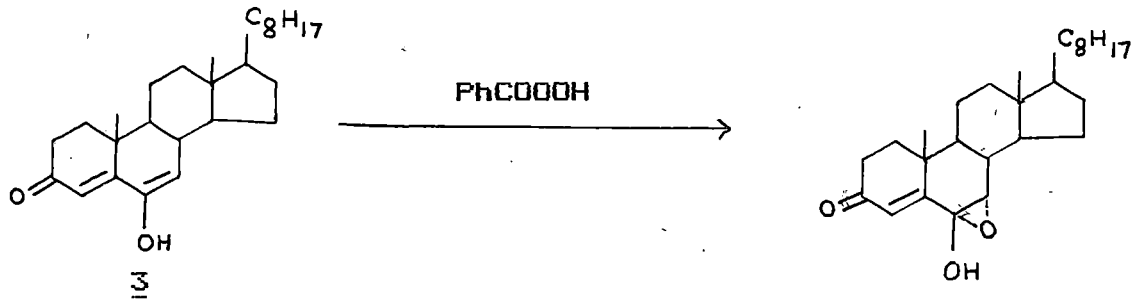


1



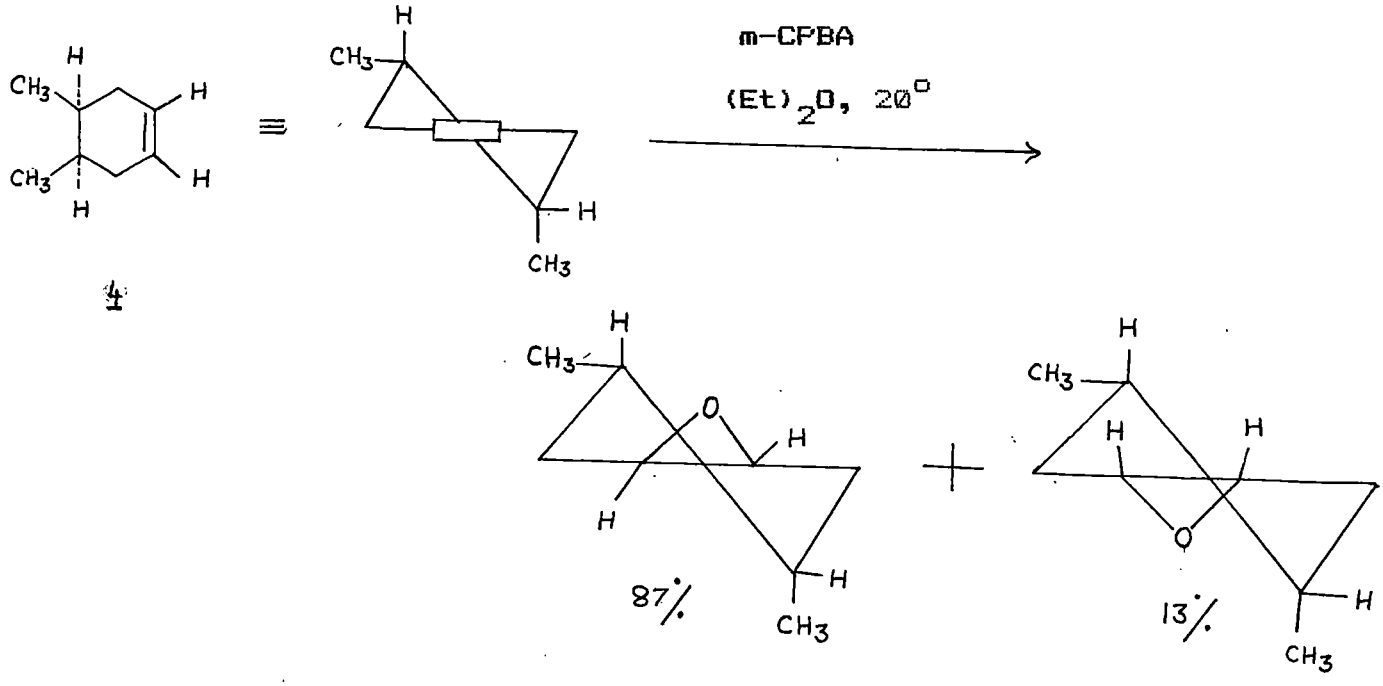
2

Carbon-Carbon double bond is selectively oxidised[3] (eg.3) in presence of hydroxyl or carbonyl functions.



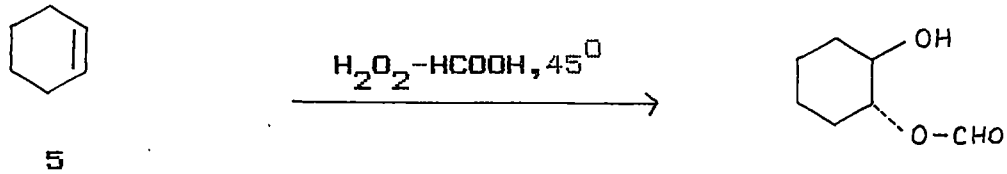
3

Rickborn et al[4] reported two different epoxide of compound 4 by action of mCPBA in diethyl ether



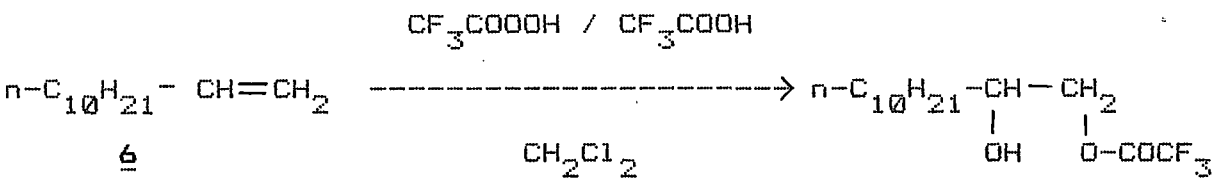
4

The use of perbenzoic acid or mCPBA in chloroform or methylene chloride has an advantage of isolating the epoxide formed while epoxidation reactions with olefin 5 run with peracids in presence of an excess of the corresponding carboxylic acid frequently yield the hydroxy esters[5] derived from the initially formed epoxide.

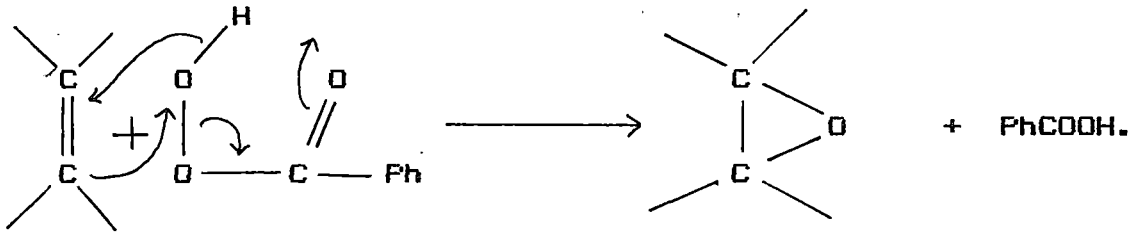


5

Reactions run either with monopermaleic acid in methylene chloride[6] or with mixtures of peroxytrifluoroacetic acid and the strongly acidic trifluoroacetic acid(P_{ka}-Ø.3) in methylene chloride[7] usually produce 1,2 diol derivatives as shown compound **6**



The epoxidation of olefins is believed to proceed by an electrophilic attack [8,9] as indicated in the accompanying equation:

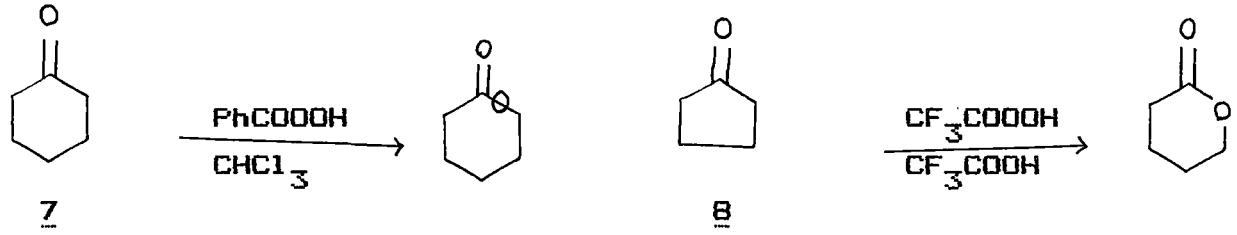


where the per acids usually attacks the olefin from the less hindered side to produce the less hindered epoxide as the major product.But the stereospecificity may be influenced by changes in the reaction solvent.[4]

OXIDATION OF CARBONYL COMPOUNDS.

The rate of oxidation of ketones with per acids is usually much slower than the epoxidation of olefins. But relatively long reaction times, strong acids as catalyst or very reactive per acids permit the conversion of carbonyl compounds, known as Baeyer-Villiger reactions[10,11,12] to corresponding esters in good yield.

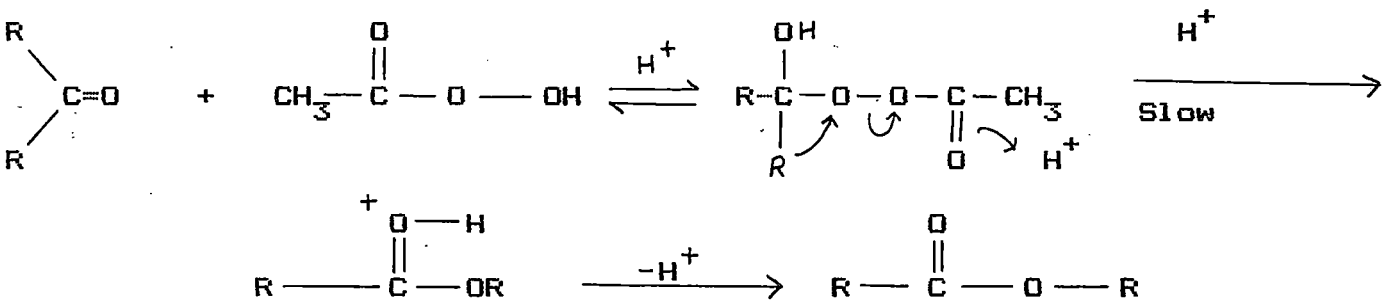
The oxidation of cyclic ketones 7 and 8, with per acids, serves as a useful route to lactones.[13,14]



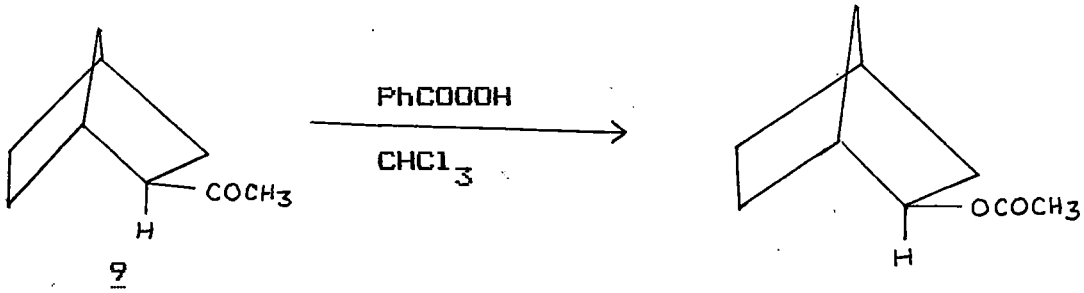
7 8

The conversion is catalysed by acids and the rate of oxidation is accelerated by electron donating groups in the ketone and electron withdrawing groups in the per acids.

After a variety of studies[12,13,15,16] of the Baeyer-Villiger reaction indicate that the mechanism is as follows:-

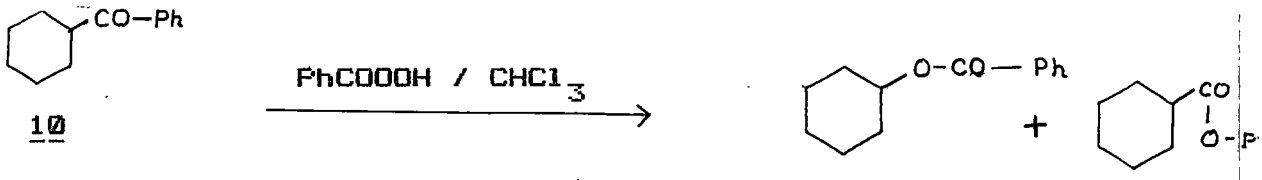


The reaction has been shown to occur with retention of configuration[17] as shown in the reaction of 9.



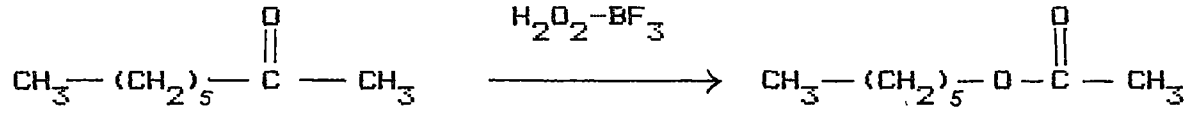
9

Oxidation of unsymmetrical ketone (eg. 10) can lead to two isomeric esters[16b]



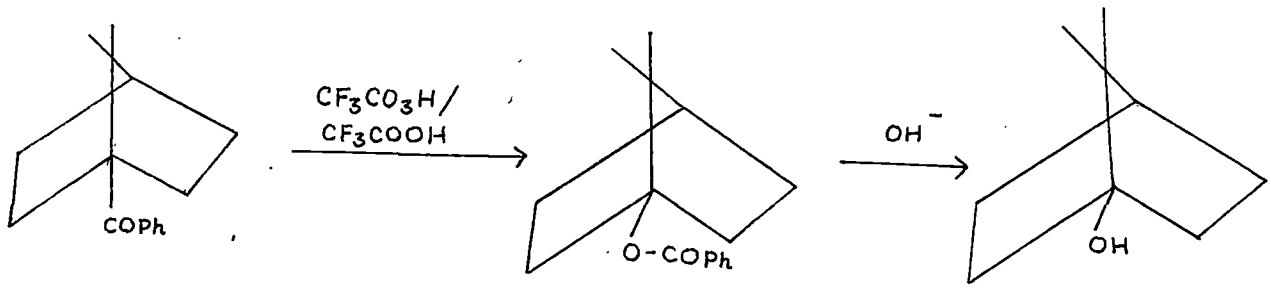
10

Mcclure et al[17e] reported B.V.oxidation by a complex of hydrogen peroxide-Boron trifluoride etherate complex.



From a series of study of various unsymmetrical ketones,[12,15,16] the migratory aptitude of various groups in the Baeyer-Villiger reaction has been found to be:-

t-alkyl > cyclohexyl ~ sec.alkyl ~ benzyl ~ phenyl > primary alkyl cyclo propyl > methyl. Even a bridgehead t-alkyl group (11) & (12) migrates readily,providing a useful synthetic route to bridgehead alcohols[15a,18]



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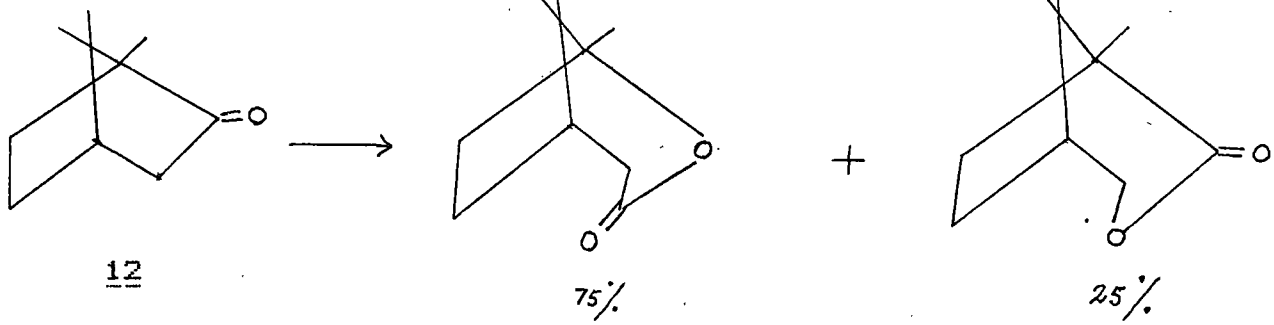


12

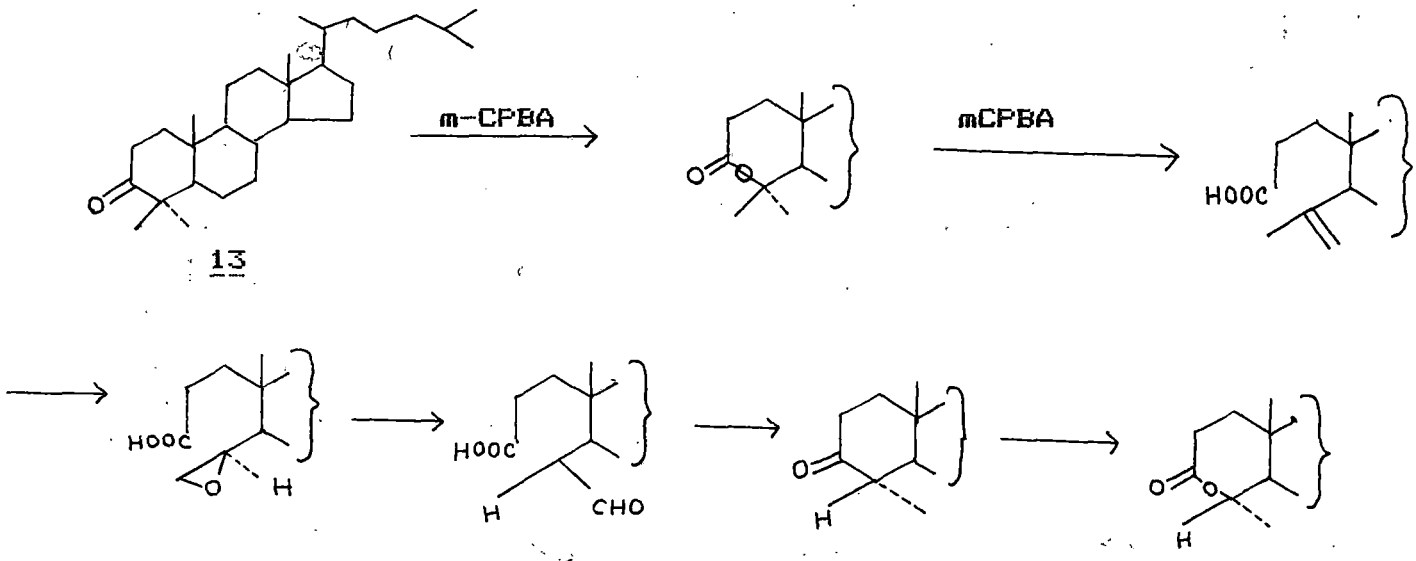
Fumio Toda et al[19] reported that some Baeyer-Villiger oxidations of ketones with mCPBA proceed much faster in the solid state than in solution.

Hara et al[20] had shown that perbenzoic acid oxidation of 5α and 5β 3-ketones yielded mixture of lactones with an oxygen atom inserted in either side of the 3-oxo group of triterpenoids with commonly used per

acids it would seen that the reaction proceeded in a rather indiscriminate manner[21].

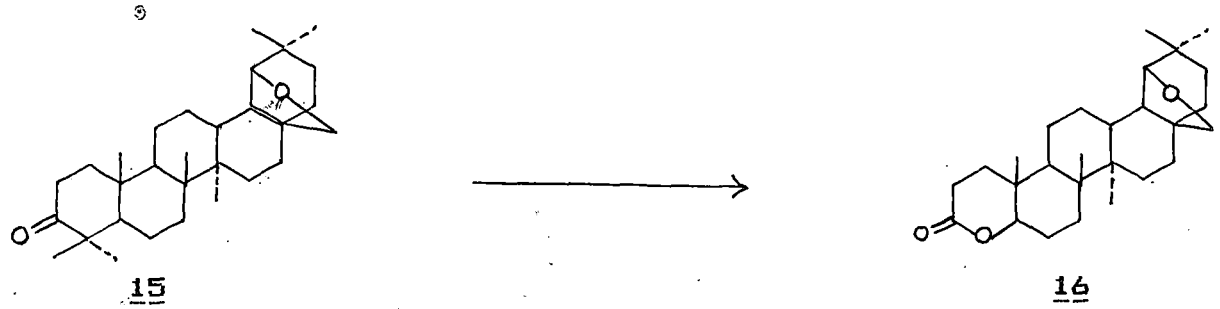
Whittam[22] found that 4,4-dimethyl cholestan 3-one **13** on treatment with mCPBA or perbenzoic acid in presence of mineral acid gave 4α methyl 4-oxa-A-homo-cholestan 3-one **14**. This apparently unique loss of a methyl group in a Baeyer-Villiger oxidation merited a careful investigation of the reaction. After careful investigation the mechanism was proposed as shown in the following scheme:-

SCHEME-I



13 **14**

Hase et al[23] reported a case of exhaustive Baeyer-Villiger oxidation of pentacyclic triterpenoid,allobetulone **15**, giving **16** in 50% yield on treatment with peracetic acid and boron trifluoride-etherate. Hase et al established that the reaction was general for condensed cyclic α,α-dimethyl substituted ketone.

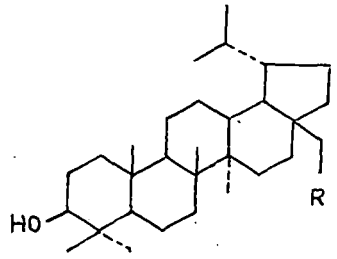


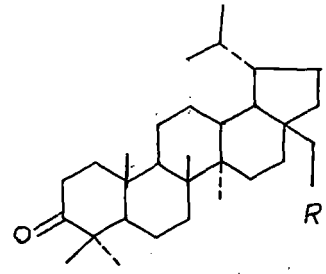
15 **16**

FUNCTIONALIZATION OF UNACTIVATED CARBON ATOM.:-

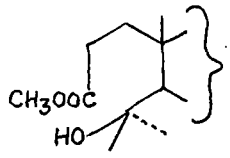
Motoo Tori et al[24] reported functionalization of unactivated carbon atoms by action of mCPBA on a number of triterpene derivatives in chloroform under reflux. They reported Lupan 3β,28 diol **17** on refluxing with mCPBA in chloroform for 6 hours afforded three compounds which were identified as 28 hydroxy lupan 3-one,**18**, methyl 4,28 dihydroxy 3,4 seco lupan 3-oate,**19** and methyl 28 hydroxy 3,4 seco lup 4(23)-en-3-oate,**20** from spectral analysis, while lupan 3β-ol, **21** on similar treatment afforded lupan 3-one,**22** and 3,4 seco lupan 4→3 olide **23**.

17, R = -OH
21, R = -H





18, R = -OH
22, R = -H



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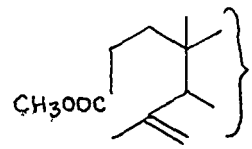

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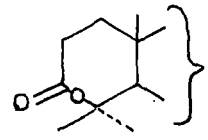


23 (4.3%)

Lupan 3β,28 diyl diacetate **24** subjected to same reaction[24] gave only one product,19β-hydroxy lupane 3β,28 diyl diacetate **25**.

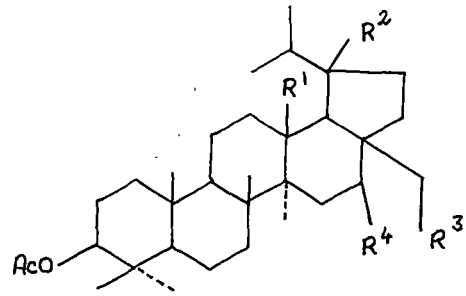
24, R_1 = R_2 = R_4 = H, R_3 = OAc

25, R_1 = R_4 = H, R_2 = OH, R_3 = OAc

26 R_1 = R_2 = R_3 = R_4 = H

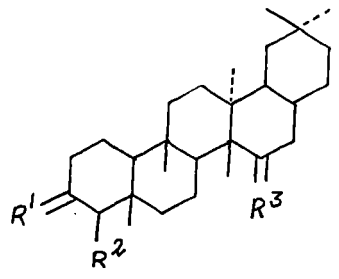
27, R_1 = OH, R_2 = R_3 = R_4 = H

28, R_1 = R_2 = R_3 = H, R_4 = OH



Lupan 3β-yl acetate, **26** on treatment[24] *with* mCPBA gave two compounds, 13β hydroxy 3β-yl acetate,**27** and 16β hydroxy 3β-yl acetate **28**.

Friedelan 3β-ol 29 on same reaction with mCPBA yielded friedelin 30, 4-epi friedelin 31 and 3,4 seco friedelin 3→4 olide 32. while-friedelin 3β-yl acetate 33 furnished only one product as 15-oxo friedelan 3β-yl acetate 34.



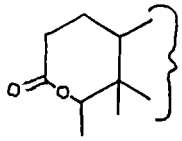
29, R_1= ; R_2= β-Me ; R_3= H_2

30, R_1= O ; R_2= β-Me ; R_3= H_2

31, R_1= O ; R_2= α-Me ; R_3= H_2

33, R_1= ; R_2= β-Me ; R_3= H_2

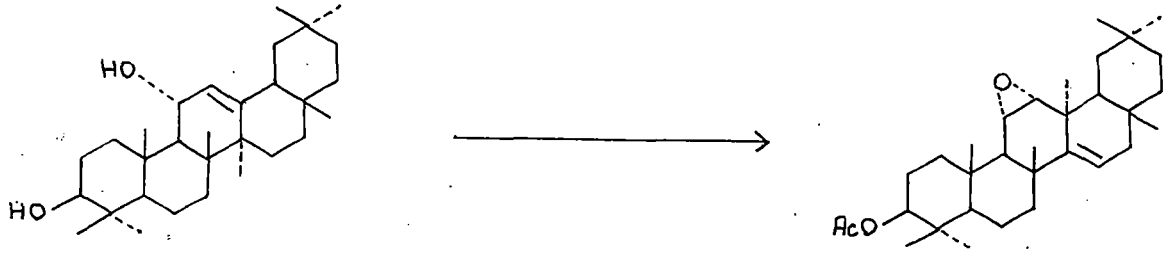
34, R_1= ; R_2= β-Me ; R_3= O



32, R_1= O ; R_2= β-Me ; R_3= H

OXIDATIVE REARRANGEMENTS

Corey et al[29] reported that 3β,11α-dihydroxy Δ^{12}-pentacyclic triterpenoid 35 on treatment in methylene chloride with a solution of H_2O_2 (30%) – p-toluenesulphonic acid in tertiary butanol, after acetylation, gave 11α,12α epoxide, 36 with a rearranged skeletal system (C_{14} C_{13} methyl migration and shift of the double bond). The free epoxy alcohol is similar to the product obtained from photoxidation of β-amyrin.

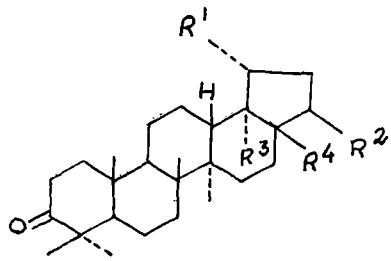


35 36

Pradhan et al[30] studied the action of mCPBA in presence of p-toluene-sulphonic acid on friedelin 30 as a member of 4-mono methyl 3-keto

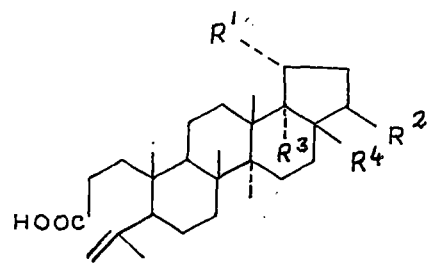
triterpenoids and lupanone 22 and moretanone 37 for 4,4 dimethyl 3-keto triterpenoids. They observed that 30 gave only a ε-lactone, 32 while 22 and 37 first furnished the corresponding ε-lactones,which being unstable due to the sterical strain from C-4 axial methyl group resulted the corresponding 3,4 seco acids 38 and 39 by opening of the ring system in situ under the influence of p-toluenesulphonic acid.

30



22, R_1= ⟨ ; R_2= H
R_3 = H ; R_4 = CH_3

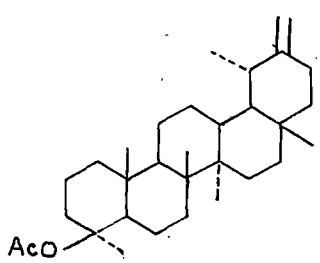
37, R_1= H ; R_2= ⟨
R_3 = CH_3 ; R_4 = H



38, R_1= ⟨ ; R_2= H
R_3 = H ; R_4 = CH_3

39, R_1= H ; R_2= ⟨
R_3 = CH_3 ; R_4 = H

Dutta et al[25] studied the action of mCPBA on taraxasteryl acetate 41 and reported three compounds formed as taraxa-20α,30α oxido-3β-yl acetate 42 and E-ring enlarged products 43 and 44.



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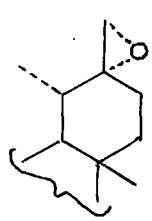

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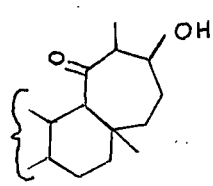
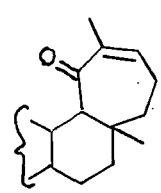
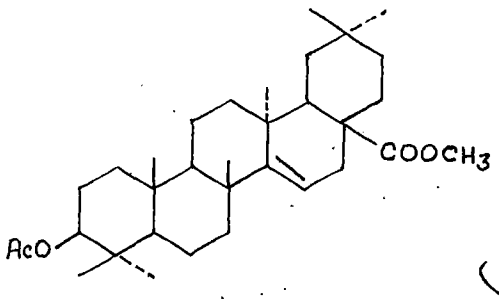


43,



44,

They[26] extended the reaction on olean-14-en-28-carbomethoxy 3β-yl acetate 45 and reported the isolation of olean 14α,15α oxido 28 carbomethoxy 3β-yl acetate 46 along with two rearranged products as olean 12-en-28-carbomethoxy 15α-hydroxy 3β-yl acetate 47 and olean 12--en-28-carbomethoxy 15-oxo-3β-yl acetate 48.



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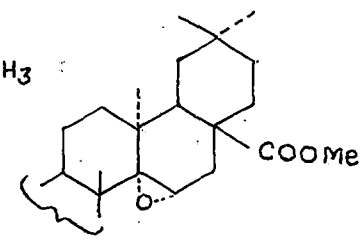

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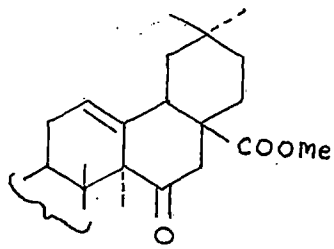

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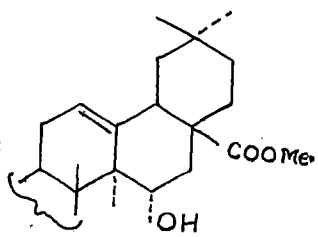
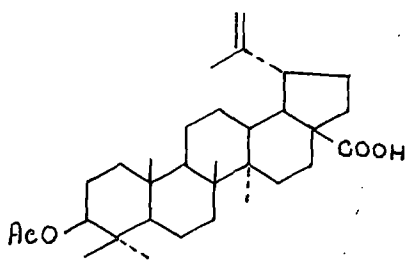


47,

Patra et al[27] studied the action of mCPBA on 3-acetylbetulinic acid 49 in dichloro methane and reported the isolation of three products as 3β-acetoxy lupan 28,29 di-oic acid 50, 3β-acetoxy 30-hydroxy lup-20 (29)-en 28-oic acid 51 and 3β-acetoxy 20-hydroxy lupan-29-al-28-oic acid 52.



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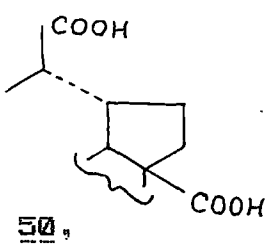
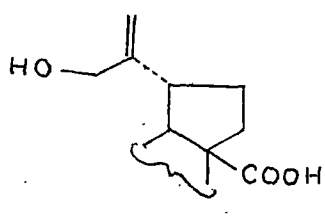
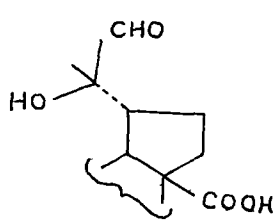


50,

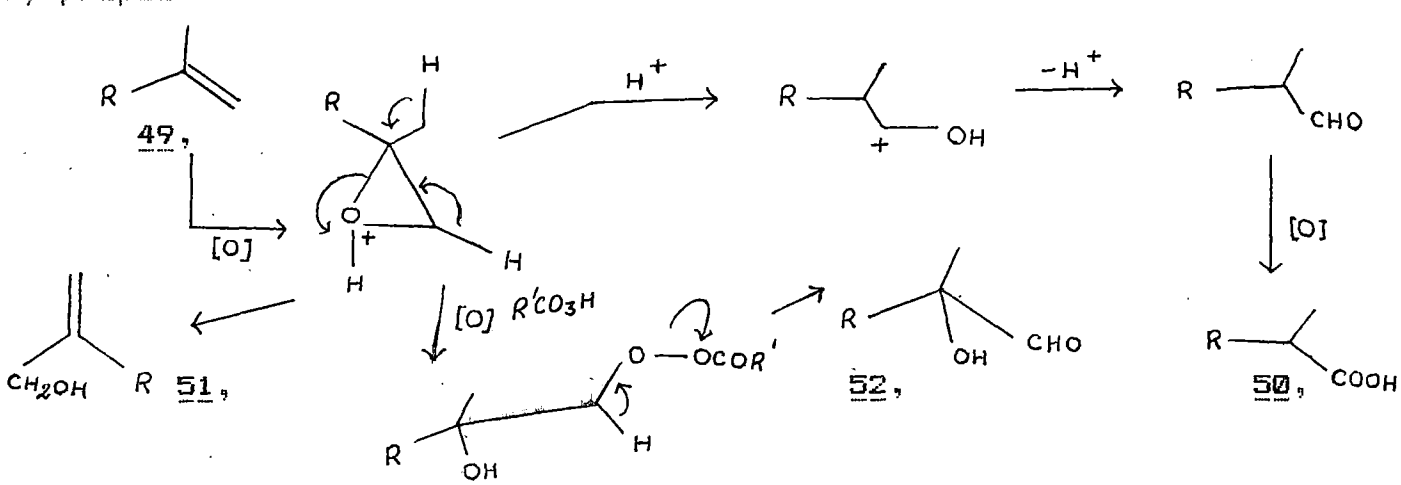


51,



52

They proposed the mechanism as shown below :-



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.

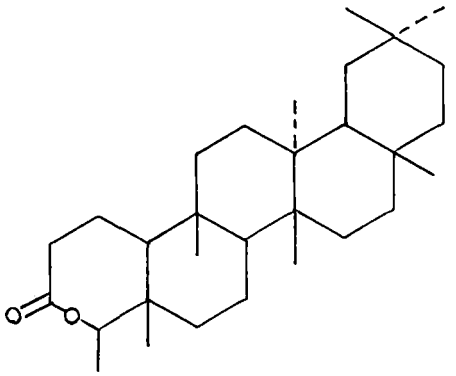
Identification of compound-A :

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 ε-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 (δ 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

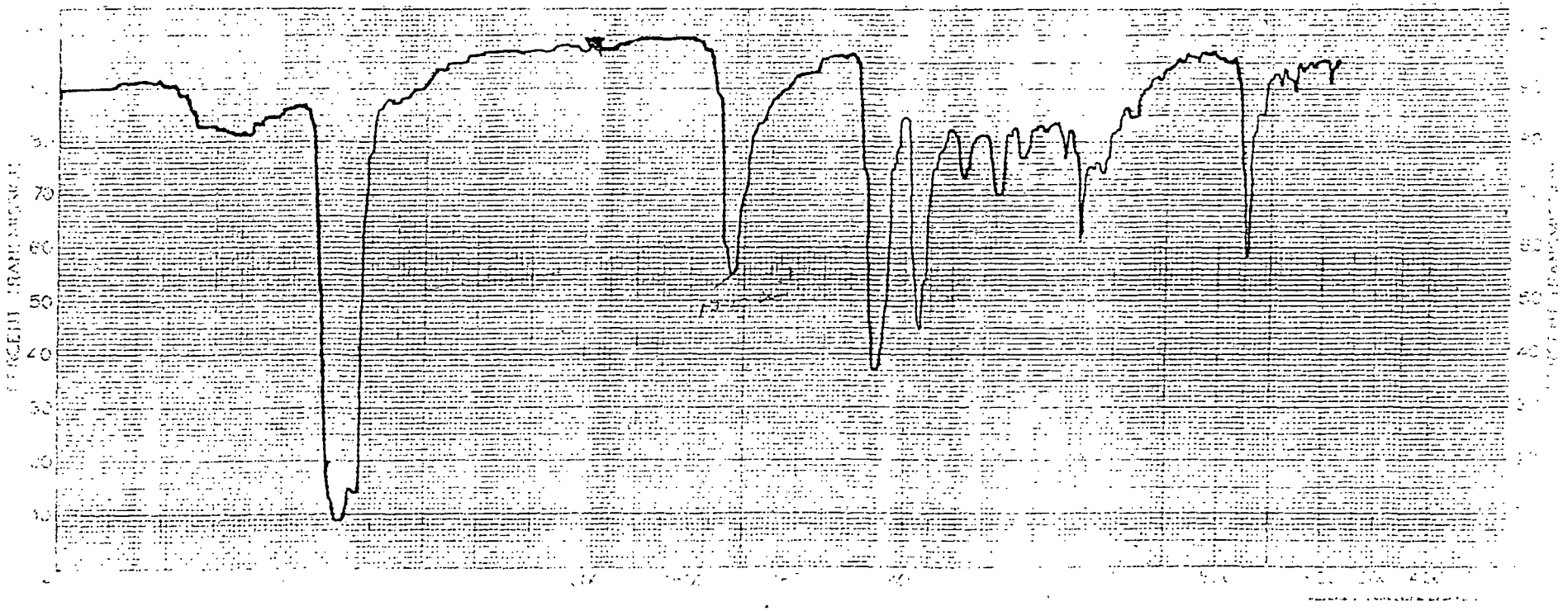


Fig. 1, IR spectrum of seco friedel-3→4-olide, 32.

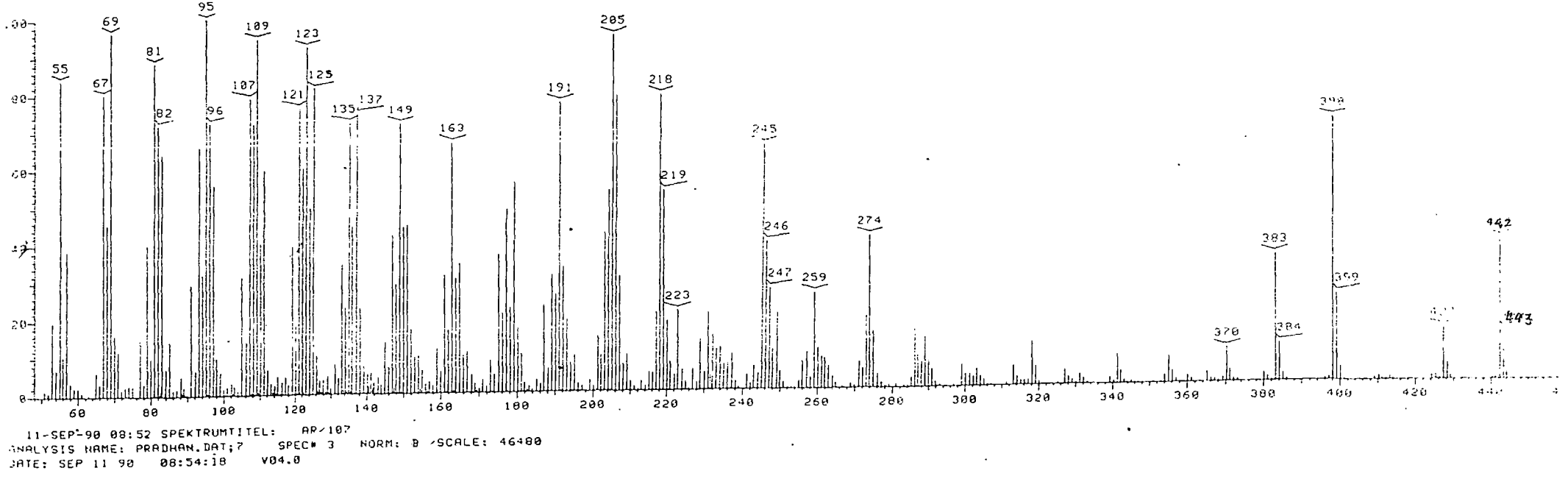


Fig. 2, Mass spectrum of seco friedel-3→4-olide, 32.

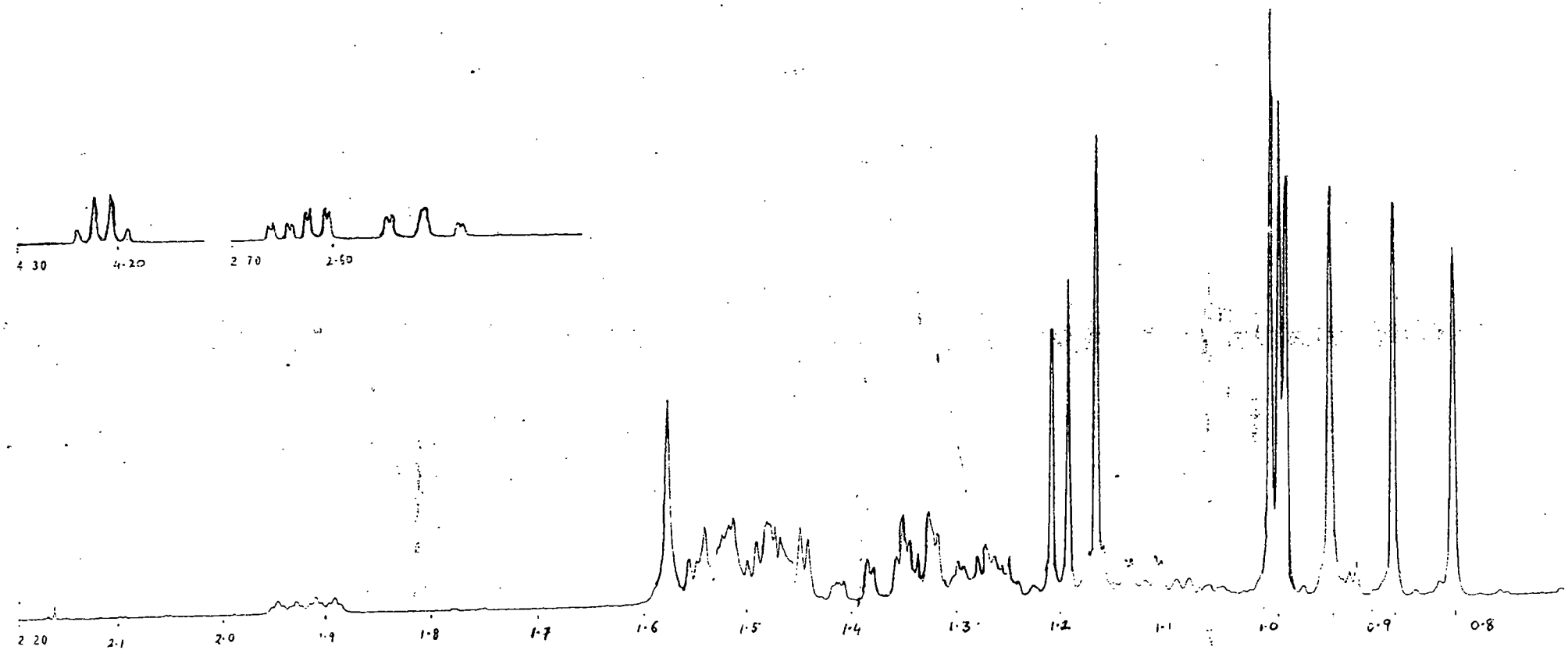


Fig. 3, ^{1}H NMR spectrum of seco friedel-3→4-olide, 32.

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 ε-lactone and γ-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. (δ in ppm.)	No. of protons.	multiplicity	Assignments.
0.85	3	singlet	
0.90	3	"	

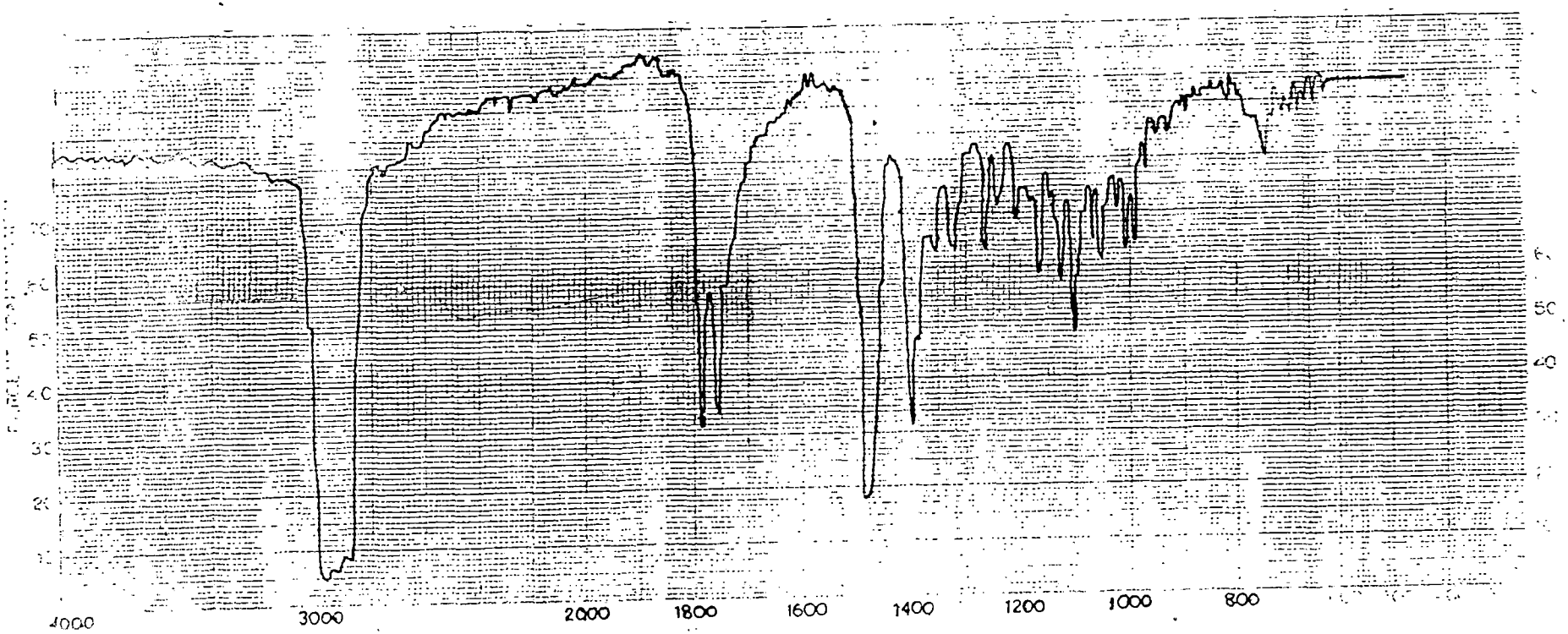


Fig. 4, IR spectrum of friedel-3→4, 27→15-di-olide, 54.

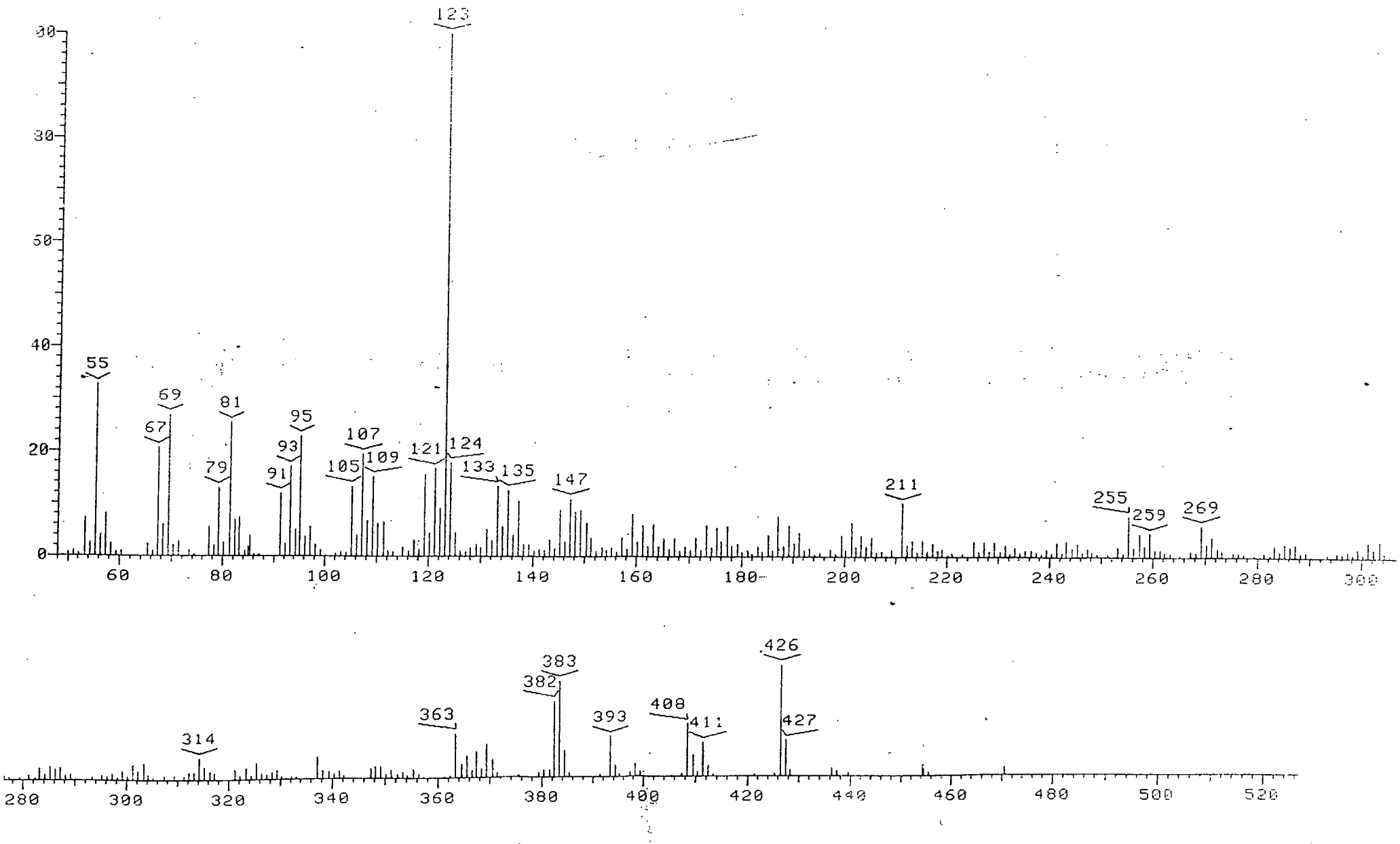


Fig. 5, Mass spectrum of friedel-3→4, 27→15-di-olide, 54.

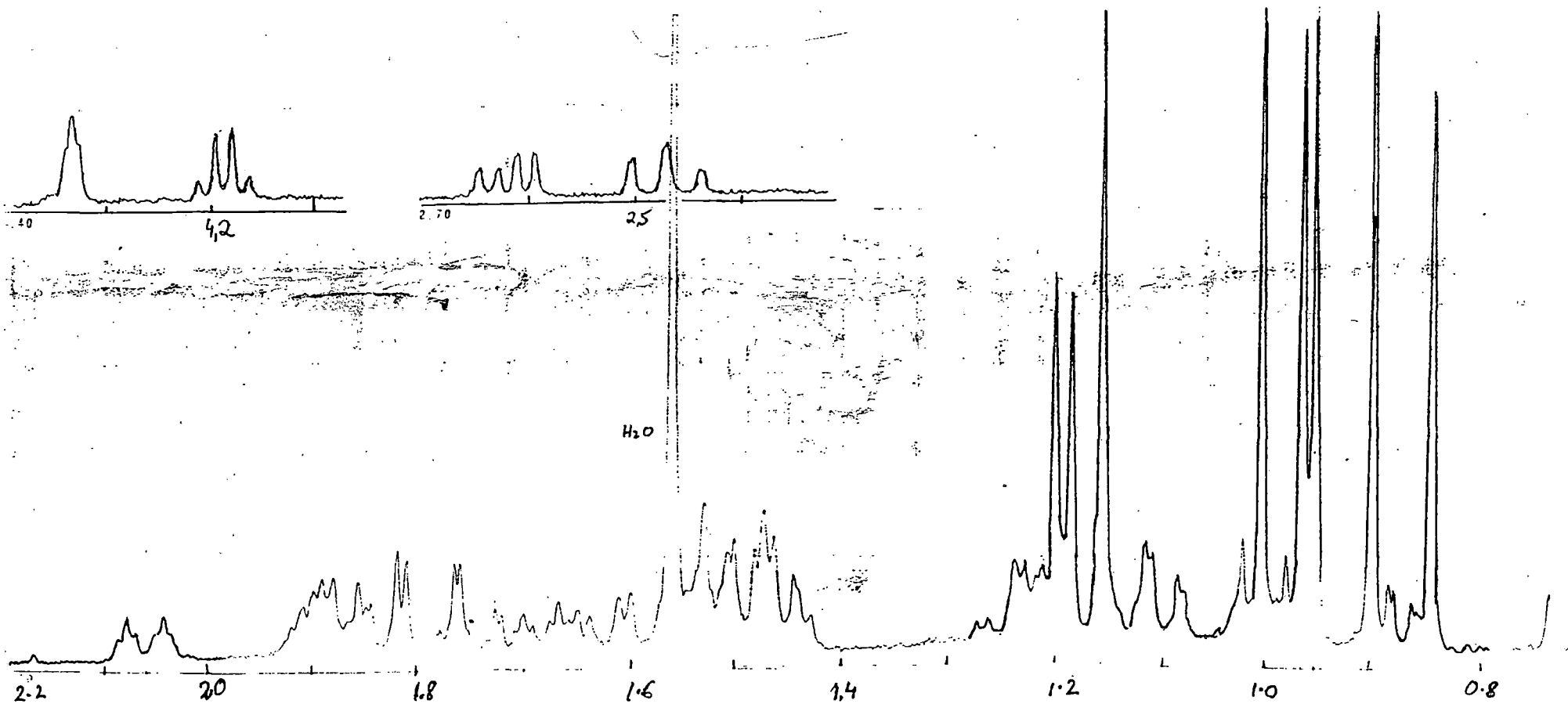
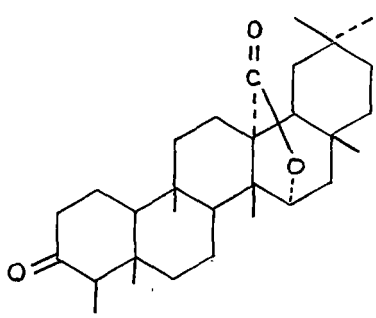


Fig. 6, ^{1}H NMR spectrum of friedel-3→4, 27→15-di-olide, 54.

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_4H-
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**.



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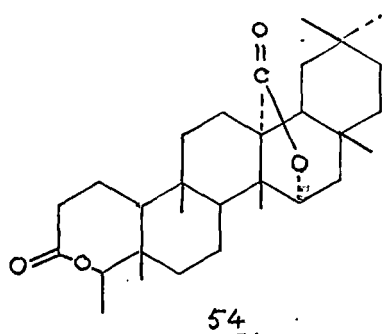


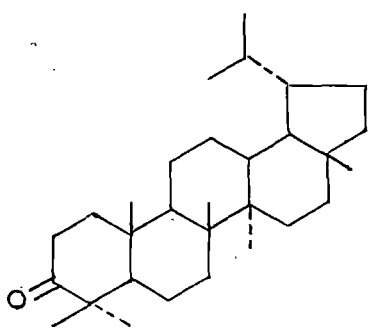
54

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]



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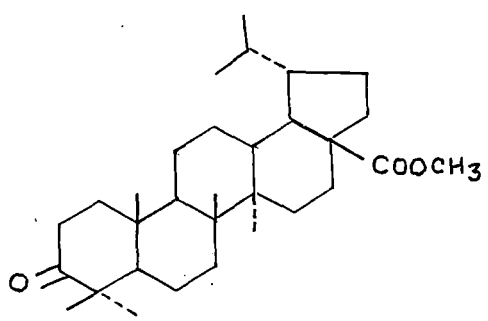


55

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 (δ 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

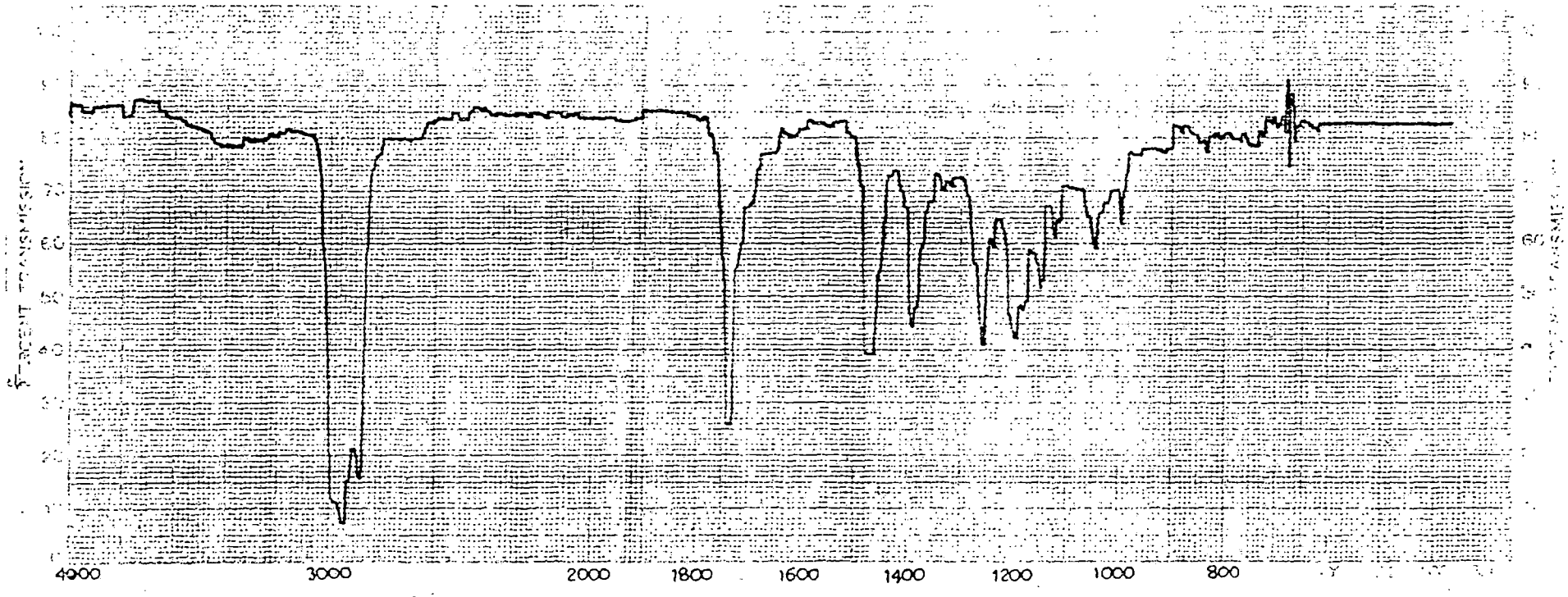


Fig. 7, IR spectrum of 29-nor 3β-O--acetyl-Lupan-20-O-formyl 28-methyl carboxylate, 57a.

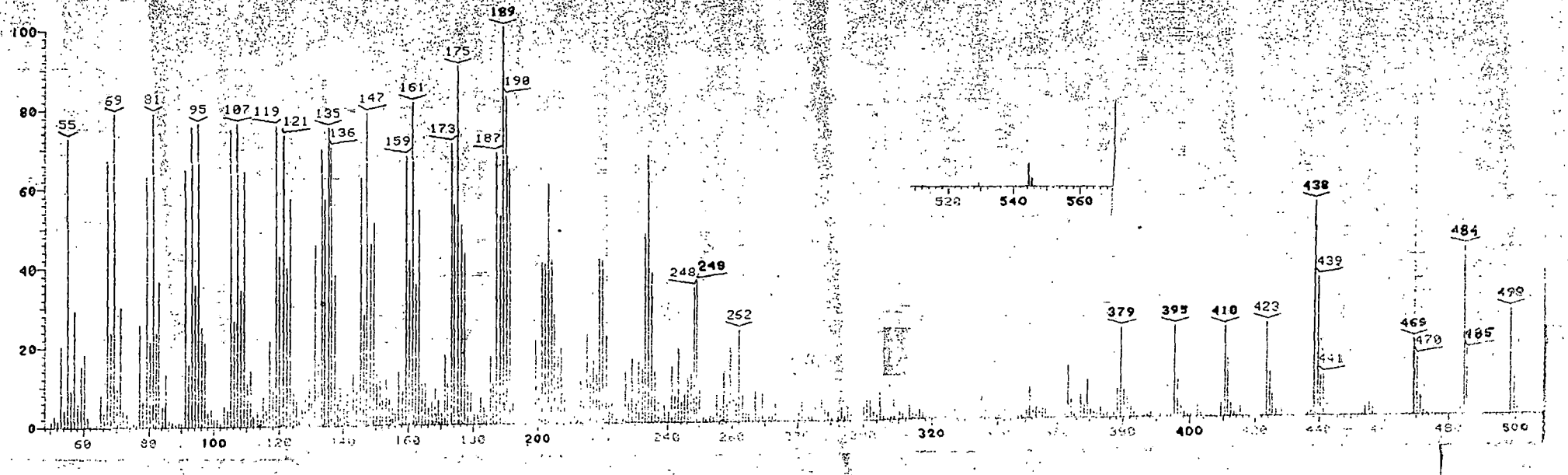


Fig. 8, Mass spectrum of 29-nor 3β-O--acetyl-Lupan-20-O-formyl 28-methyl carboxylate, 57a.

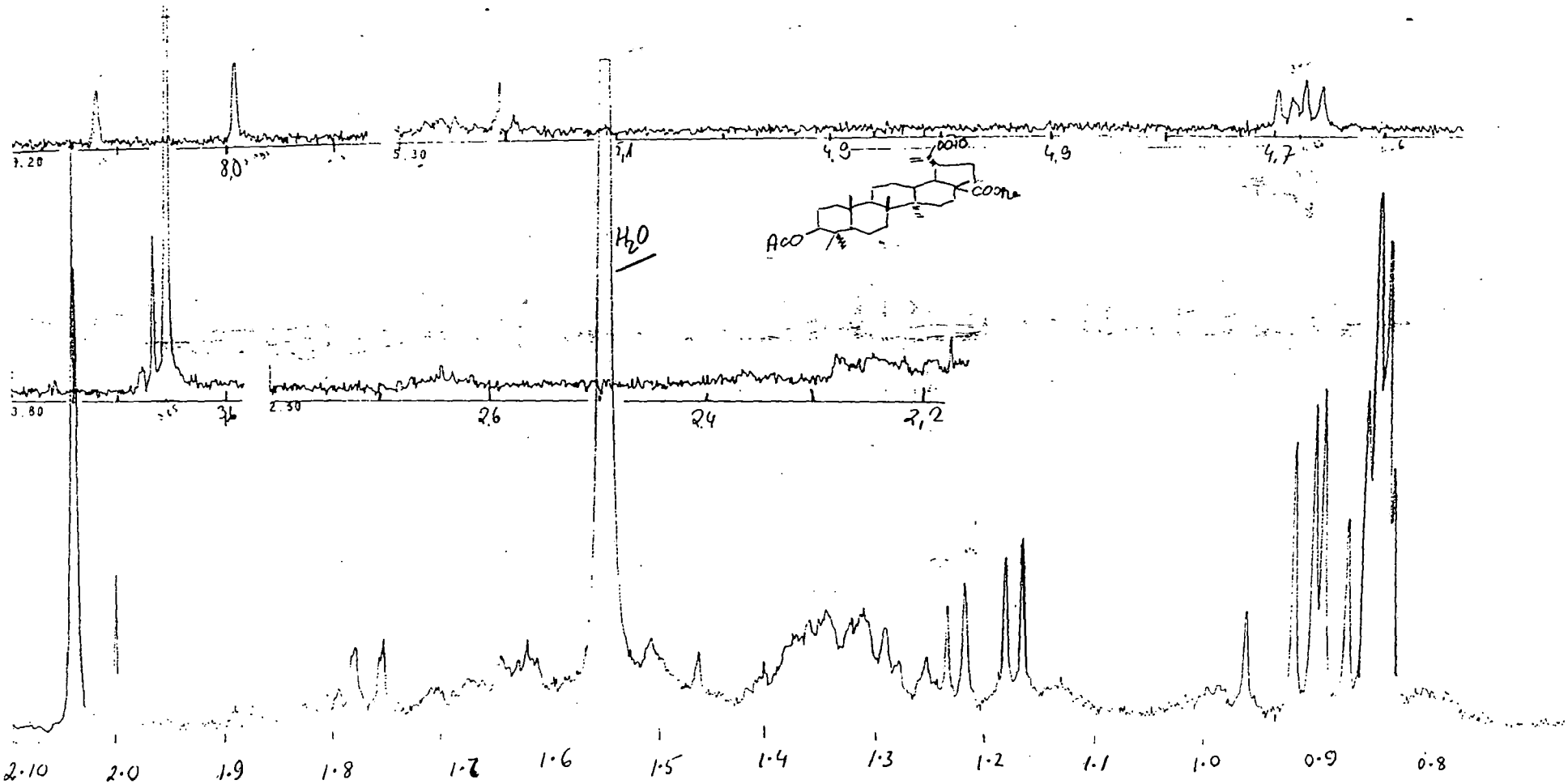
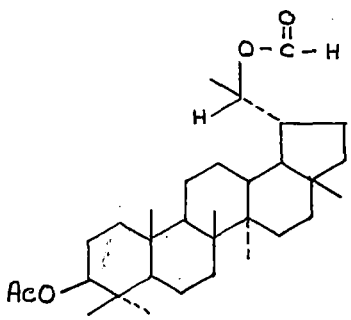


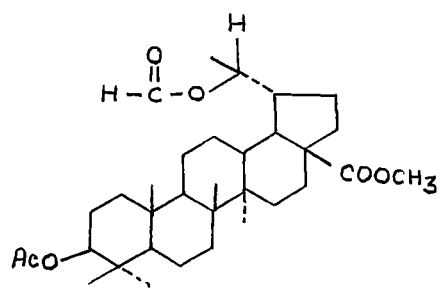
Fig. 9, ^{1}H NMR spectrum of 29-nor 3β-O--acetyl-Lupan-20-O-formyl 28-methyl carboxylate, 57a.

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.

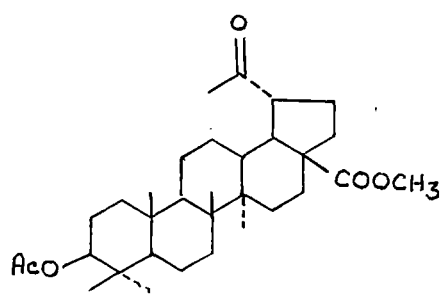
Thus, from all the above spectral analysis the structure can be awarded to compound-C as 29-nor 3β-O-acetyl-lupan-20-O-formyl-28-methyl carboxylate **57a**.



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

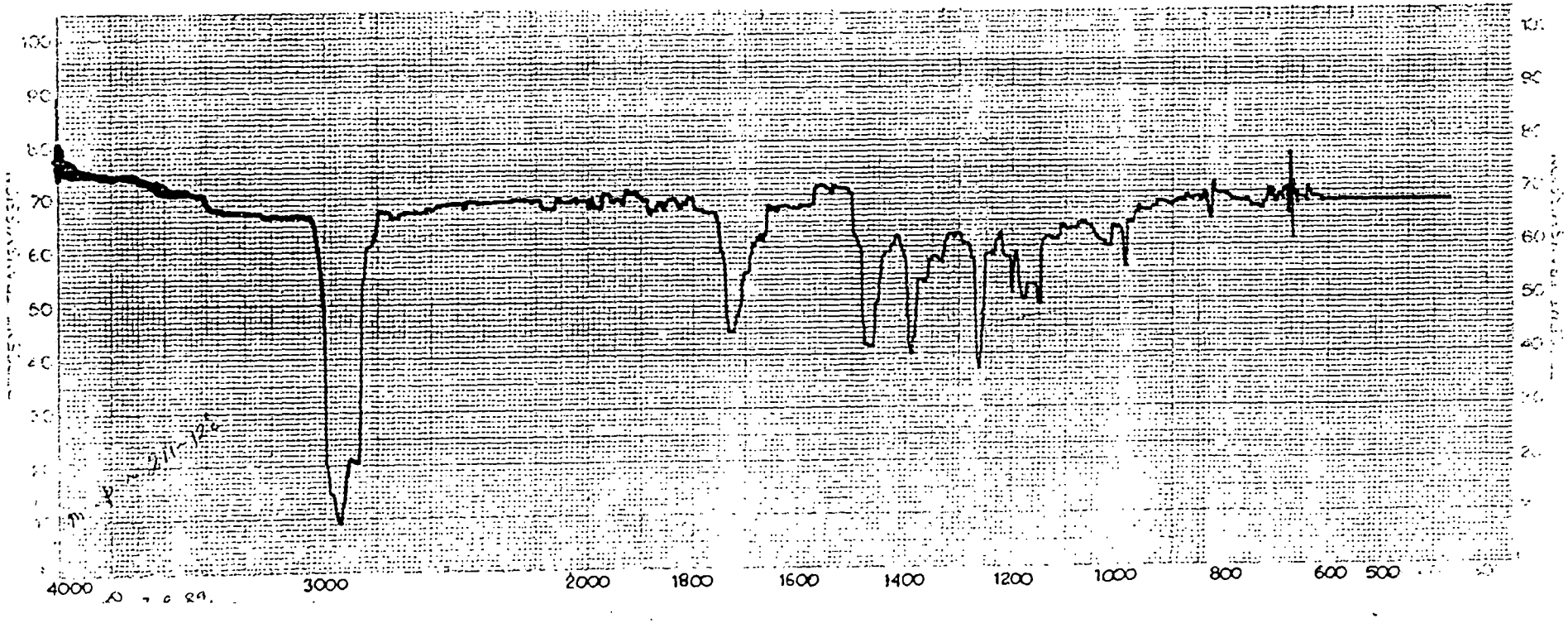


Fig.10, IR spectrum of 29-nor-acetyl,methyl,20-oxo, betulinate, 58.

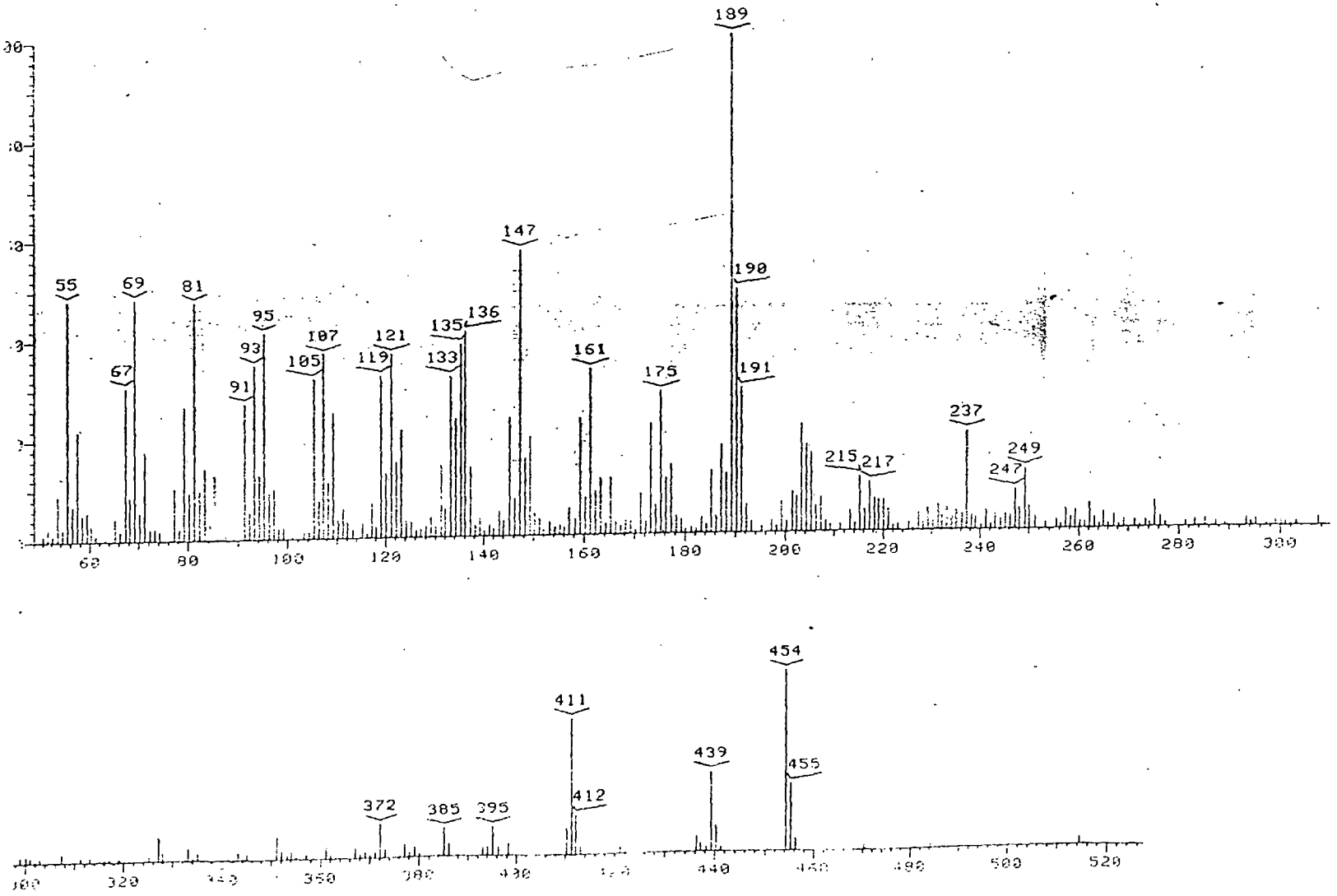


Fig.11, Mass spectrum of 29-nor-acetyl,methyl,20-oxo, betulinate, 58.

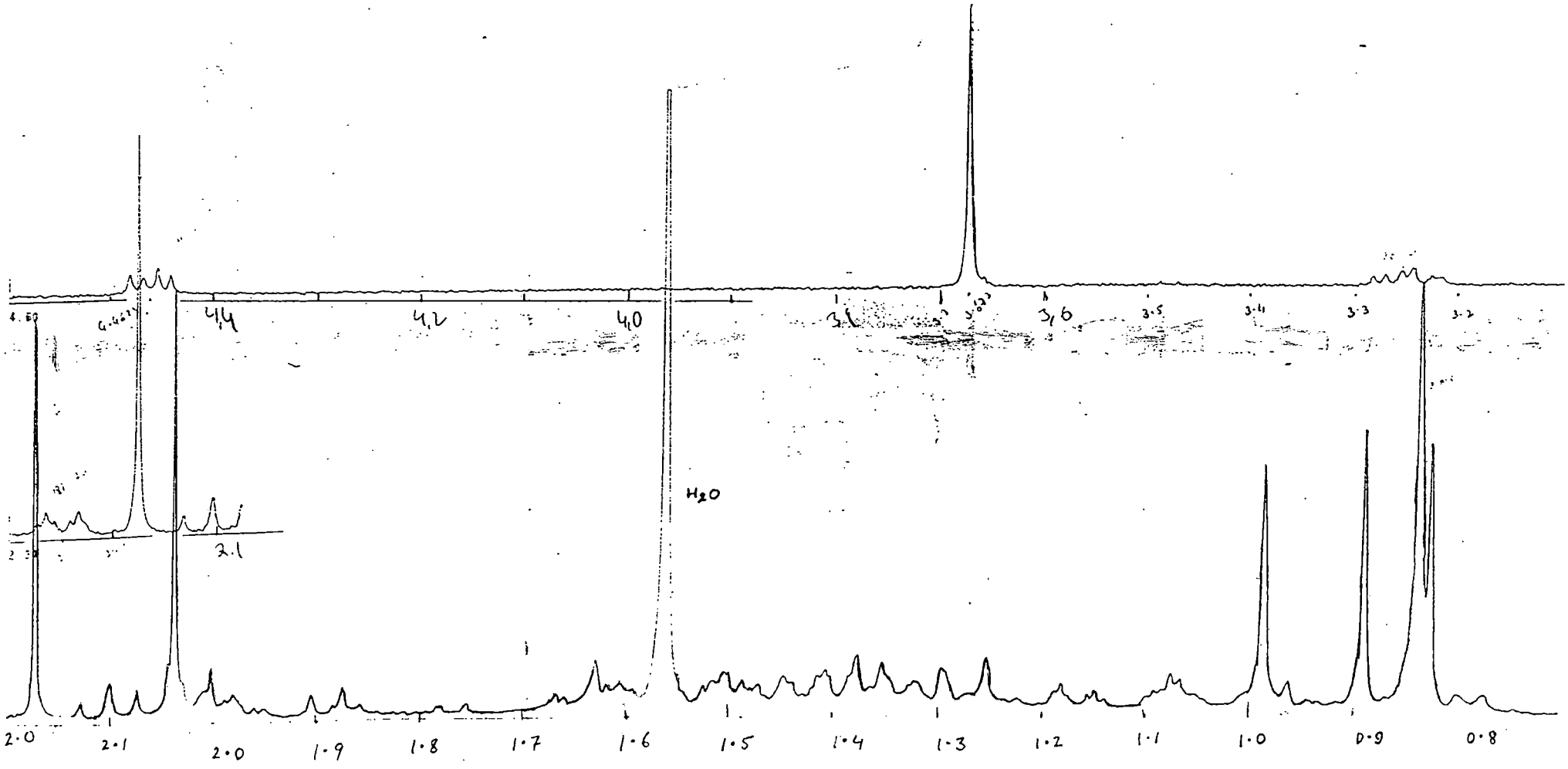


Fig.12, ^{1}H NMR spectrum of 29-nor-acetyl,methyl,20-oxo, betulinate, 58.

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.

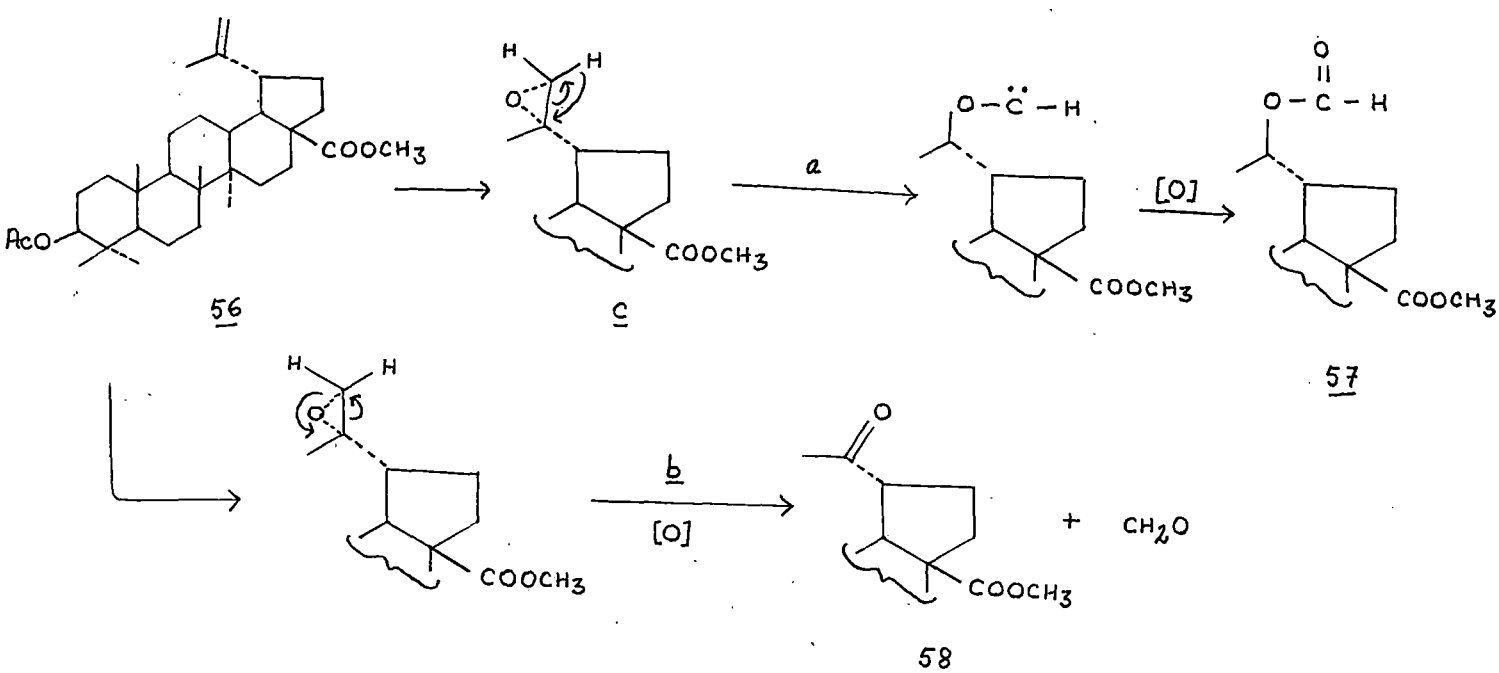
The absence of methylene protons and the C-30 methyl protons present in the starting compound **56** in which place the appearence of an additional CH_3CO group with an α-proton to the acetyl group at 3.3 ppm as a multiplet suggest that the C-29 carbon is replaced by the oxygen atom to form the carbonyl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



OXIDATION OF FRIEDELIN TO FRIEDELAN 3→4-OLIDE BY M-CHLOROPERBENZOIC ACID (m-CPBA) IN CHLOROFORM.

0.5 g of friedelin **30** was dissolved in 100 ml. $CHCl_3$ and 0.5 g of m-CPBA was added. The mixture was then refluxed over waterbath for 6 hours and allowed to cool at room temperature. Than it was diluted with 100 ml. of $CHCl_3$ and was washed with 5% of Na_2CO_3 solution there by separating into $CHCl_3$ and alkali layer. The $CHCl_3$ layer was washed with water repeatedly till neutral, dried over anhydrous Na_2SO_4 and the solvent was distilled off yielding a solid mass. It was dissolved in minimum volume of benzene and chromatographed over silica column.

The result of elution with solvents are given below in table-I.

TABLE-I

	Eluent	Fraction of 50 ml each.	Residue on distillation.
1.	petrol	1-4	nil.
2	petrol-benzene (4:1)	5-9	nil.
3.	petrol-benzene (3:2)	10-16	solid (0.4 g)

Further continuation did not afford any more solid.

The fractions 10-16 were crystallised together from $CHCl_3$-MeOH, *M.P.* 271-2°C; identified as 3,4 seco friedelan 3→4-olide **32**.

ANALYSIS REPORT.

Found : C 80.7 ; H 10.9%

Calculated for $C_{30}H_{50}O_2$: C 81.0 ; H 11.0%

IR (Nujol) : ν_{max} 1720 cm^{-1} (ε-lactone) fig.1.

Mass : m/e	442 (M^+), 427, 398, 383, 274, 245, 218, 205, 123, 109, 95 (100).

fig.2

^1H NMR : ($CDCl_3$) (δ in ppm)	0.82, 0.88, 0.93, 0.98, 0.99, 1.00 and 1.18. (7s, 21H, 7X t-CH_3)
	1.20 (d, J=6.5 Hz, CH_3-C_4H)
	2.60 (m, methylene at C-2)
	4.23 (q, J=6.5, C_4H-CH_3)

fig.3

TREATMENT OF ALKALI PART :-

The aqueous alkali part was acidified with 20% HCl when a white solid separated out. It was filtered, washed with water and dried. This was found to be m-chlorobenzoic acid by comparing with authentic sample (IR, *M.M.P.* and Co-tlc)

OXIDATION OF 3-OXO-FRIEDALAN 27→15-OLIDE **53** *WITH* mCPBA :-

0.5 g of 3-oxo-friedelan 27→15-olide **53** was dissolved in 100 ml.$CHCl_3$ and 0.5 g of mCPBA was added. The mixture was refluxed for 6 hours and after workup, the neutral $CHCl_3$ layer yielded a gummy substance while aqueous alkali part gave only m-chlorobenzoic acid.

The gummy mass was dissolved in minimum volume of benzene and chromatographed. The solvent used are given in table-II below-

TABLE-II

	Eluent	Fraction of 50 ml each.	Residue on distillation.
1.	petrol	1-4	nil.

2	petrol-benzene (4:1)	5-9	nil.
3.	petrol-benzene (3:2)	10-14	nil.
4.	petrol-benzene (1:4)	15-20	solid.

The fraction 15-20 were combined and crystallised from $CHCl_3$-MeOH, *M.P.* >300°C; identified as friedelan 3→4,27→15 di-olide **54**.

ANALYSIS REPORT.

Found :	C 76.01 ; H 9.15%
Calculated for $C_{30}H_{46}O_4$:	C 76.59 ; H 9.70%
IR (Nujol) : ν_{max}	1730 and 1760 cm^{-1} (C=O of ε and γ-lactone moiety.) fig.4
Mass : m/e	470 (M^+), 426, 408, 383, 363, 123 (100). fig.5
^1H NMR : ($CDCl_3$) (δ in ppm)	0.85, 0.90, 0.95, 0.96, 1.00 and 1.16 (6s,18H,6X t-CH_3) 1.20 (d,J=6.5 Hz,CH_3-C_4H) 2.46 (m,1H, 2α-H) 2.63 (m,1H,2β-H) 4.19 (q, CH_3-C_4H) 4.35 (t,J=3 Hz,15β-H) fig.6

OXIDATION OF ACETYL METHYL BETULINATE **56** *WITH* m-CPBA *IN* $CHCl_3$.

1.0 g of acetyl methyl betulinate **56** was dissolved in 100 ml. $CHCl_3$ and 1.0 g of m-CPBA was added. The mixture was than refluxed for

6 hours and allowed to cool at room temperature. After usual workup, the neutral $CHCl_3$ layer yielded a gummy white mass while the alkali layer gave m-chlorobenzoic acid.

The gummy mass which showed to distinct spots on tlc plates was dissolved in minimum benzene and chromatographed over silica gel. The results are given in the table-III below-

TABLE-III

	Eluent	Fraction of 50 ml each.	Residue on distillation.
1.	petrol	1-4	nil.
2	petrol-benzene (4:1)	5-8	nil.
3.	petrol-benzene (3:2)	9-12	nil.
4.	petrol-benzene (2:3)	13-15	nil.
5.	petrol-benzene (1:4)	16-20	solid. (0.2 g)
6.	benzene	21-24	nil.
7.	benzene-chloroform (4:1)	25-30	solid. (0.35 g)

Further elution did not afford any more solid.

Fractions 16-20 were crystallised together from $CHCl_3$-MeOH, *M.P.* 151-2°C; identified as lupan 20-formato,28-carbomethoxy 3β-yl acetate 57.

ANALYSIS REPORT

Found :	C 72.10 ;	H 10.41%
Calculated for $C_{33}H_{54}O_6$:	C 72.24 ;	H 10.72%

IR (Nujol) : ν_{max} 1740 and 1250 cm^{-1}
($-COOCH_3$ and $-O-COCH_3$)

fig.7.

Mass : m/e 544 (M^+), 498, 484, 438, 423, 410, 395, 379, 249, 189 (100).

fig.8.

^1H NMR : ($CDCl_3$) 0.80-0.96 (5s,15H,5X t-Me), 3.65 (s,3H,$-COOCH_3$)
(δ in ppm.) 1.2 (dd,J=7 Hz,$-CH-CH_3$), 4.67 (m,1H, $C_3-\alpha H$)
2.04 (s,3H,$-OCOCH_3$), 7.99 and 8.12
(ss,1H,-O-CHO).

fig.9

Similarly, fractions 25-30 were collected and crystallised from $CHCl_3$-MeOH, *M.P.* 211-2°C; it was identified as 29-nor-acetyl methyl 20-oxo-betulinate **58**.

ANALYSIS REPORT.

Found : C 74.30 ; H 10.21%
Calculated for $C_{32}H_{50}O_5$: C 74.70 ; H 10.50%

IR (Nujol) : ν_{max} 1730 (broad) and 1260 cm^{-1}
($-COCH_3$,$-OCOCH_3$ & $-COOCH_3$)

fig.10.

Mass : m/e 514 (M^+), 454, 439, 411, 395, 372, 237, 190, 189 (100)

fig.11.

^1H NMR : ($CDCL_3$) 0.83,0.84,0.89,and 0.99, 3.2-3.3 (ddd,1H,J=4 Hz,
(δ in ppm) (4s.9H+6H, 5Xt-CH_3) $-C_{19}-H$)
2.03 and 2.17 3.67 (s,3H,$-COOCH_3$)
(2s,$-COCH_3$,$-OCOCH_3$) 4.46 (m,1H,$-C_3-\alpha H$)
2.25 (t,1H,J=3 Hz,-CH-)

fig.12.

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PART-IV

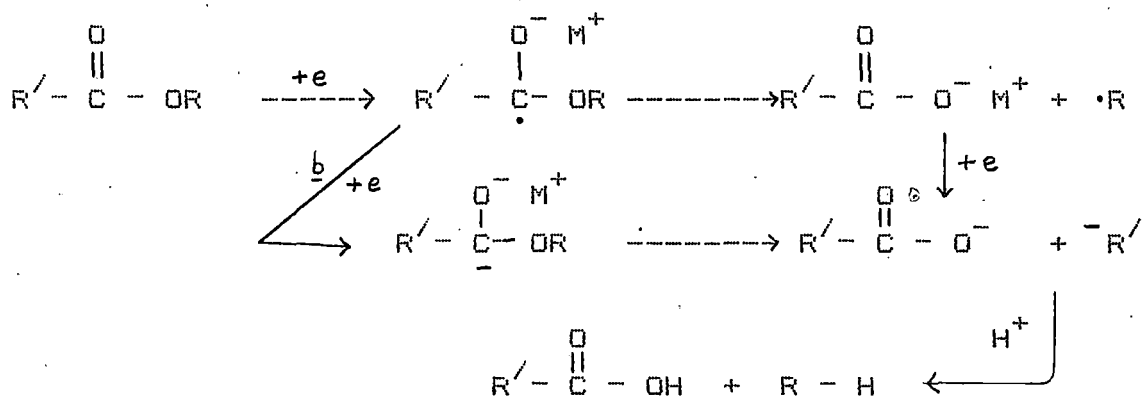
REDUCTIVE CLEAVAGE OF SEVEN MEMBERED LACTONE RING WITH LITHIUM IN ETHYLENEDIAMINE.

CHAPTER-I

A SHORT REVIEW OF LITHIUM ETHYLENEDIAMINE AS A REDUCING AGENT.

Reggel and co-workers[1] used Lithium(Li) Ethylenediamine (EDA) at 90-100°C as a potential reducing agent. Barton et al[2] showed that the esters of tertiary acids furnished acids on reduction with alkali metal amine. They proposed the mechanism as shown in scheme-I.

SCHEME-I



Likewise Sengupta et al[3] converted the C-17 carbomethoxy group of triterpenoids in to carboxylic acids on treatment with Li-EDA. Pradhan et al[4] performed a systematic study on the reduction of triterpenoids with Li-EDA and reported the wide applicability of this system in the reduction of ketones and aldehydes to alcohols, isopropenyl groups to isopropyl groups and esters of hindered acids to carboxylic acids, on a series of triterpenoids containing one or more of these functional groups as shown in the following table.

TABLE-I.

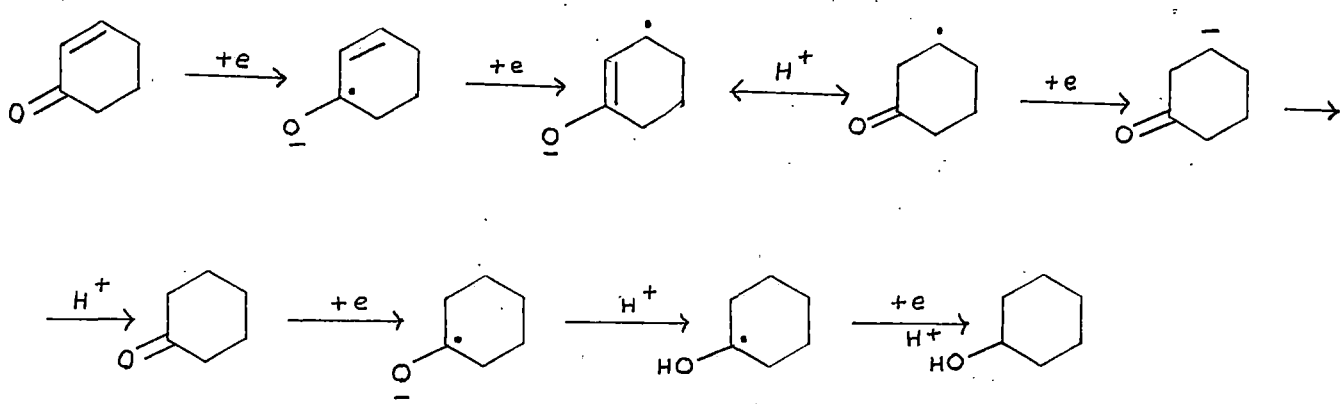
Reduction of ketones, aldehydes, isopropenyl group and esters of hindered carboxylic acids belonging to a series of triterpenoids.

ENTRY	TRITERPENOIDS	PRODUCTS	FUNCTIONAL GROUPS REDUCED
1.	*Lupanone*[6]	*Lupanol*[6]	C=O

2.	*Friedlin*[6]	*Friedelinol*[6]	C=O
3.	*Betulonic* aldehyde[6]	*Dihydrobetulin*[6] C=O,	CHO, $C=CH_2$
4.	*Oleanonic alhedyde*[6]	*Erythrodiol*[6]	C=O, CHO.
5.	*Lupeol*[6]	*Lupanol*[6]	$C=CH_2$
6.	*Moretenol*[7]	*Moretanol*[7]	$C=CH_2$
7.	*Lupenone*[6]	*Lupanol*[6]	$C=CH_2$, C=O,
8.	*Methyl aleuritolate*[9]	*Aleuritolic acid*[9]	COOMe.
9.	*Methyl trichadinate*[10]	*Trichadenic acid*[10]	COOMe
10.	*Methyl oleanonate*[8]	*Oleanolic acid*[8]	C=O, COOMe
11.	*Methyl Urosonate*[8]	*Ursolic acid*[8]	C=O, COOMe
12.	*Methyl betulonate*[6]	*Dihydrobetulinic acid*[6]	$C=CH_2$, CO, and COOMe.

Pradhan et al[4b] proposed the mechanism as shown in scheme-II.

SCHEME-II



Lactones may be considered as intramolecular esters which are formed by condensation of hydroxy groups with carboxylic acid functions of the same molecule.Therefore it was envisaged that lactone oxygen might be cleaved from its point of attachment by the action of Li-EDA..This application of lithium - ethylenediamine on lactones obtained from the bark of *Gynocardia Odorata*,[5] for reductive cleavage of their lactone rings had been sucessful.[5] The results of several such reactions are shown in table-II.

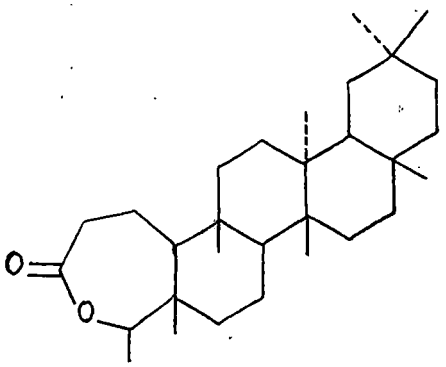
TABLE-II

Substrate lactones.	Product.	Yield.
1.3α-hydroxy friedelan 27→15α-olide.	3α-hydroxy friedelan 27-oic acid	80%
2.3α-acetoxy friedelan 27→15α-olide.	(a).Friedelan 27-oic acid.	40%
	(b).3α-hydroxy friedelan 27-oic acid.	40%
3.3-oxo-friedelan 27→15α-olide. (odolactone)	3α-hydroxy friedelan 27-oic acid	80%
4.Friedelan 27→16α -olide. (Iso-deoxyodolactone)	(a) Friedelan 27-oic acid.	20%
	(b) Friedelan 16α,27 -diol	60%
5. Friedelan 27→15α -olide. (Deoxyodolactone)	Friedelan 27-oic acid.	80%
6. 3β-acetoxy oleanan 18α-H,28→13β-olide.[8]	(a) Oleanan 18α-H,28 -oic acid.	40%
	(b) 3β-hydroxy oleanan-18α-H,28-oic acid.	40%
7. 3β-acetoxy oleanan 18α-H,28→19β-olide.[8]	(a) Oleanan 18α-H,28 -oic acid.	30%
	(b) 3β-acetoxy oleanan-18α-H,28-oic acid.	30%
	(c) Oleanan 18α-H,3β,19β, 28-triol.	15%

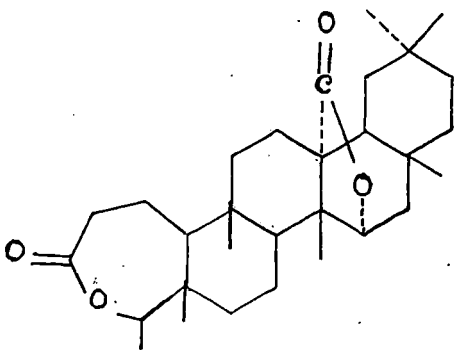
All the above products were characterised from their spectral data.

From the above observations it can be concluded that five membered lactones (1 to 7)on reductive cleavage with lithium-ethylene

diamine furnished the corresponding acids in all but one (7c) cases. So, presently the author was interested to see the effect of Lithium-ethylene diamine on seven membered lactone ring compounds and have chosen 3,4 seco-friedelan 3→4 olide 1 and 3,4 seco-friedelan 3→4, 27→15α di-olide 2 as the substrate.

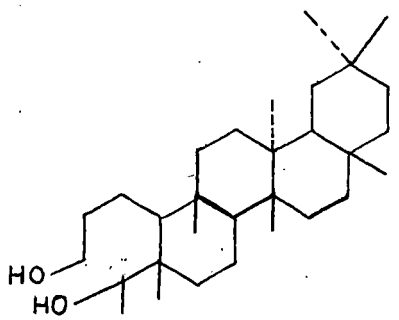


1



2

Both the compounds 1 and 2 on reduction with lithium ethylenediamine (the latter was carried out at room temperture to keep the five membered lactone moiety intact) produced diol exclusively.



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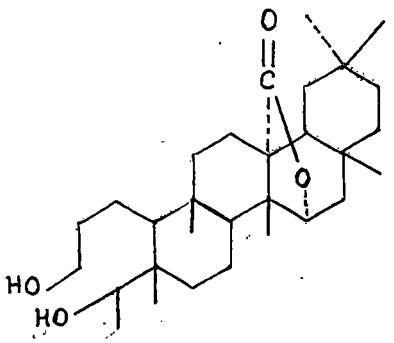


4

The two diols 3 and 4 were identical with the products obtained from LAH reduction of compounds 1 and 2.

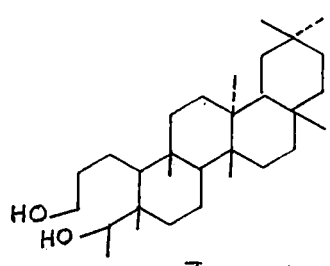
REDUCTIVE CLEAVAGE OF 3 4 SECO FRIEDELAN 3 4-OLIDE WITH LITHIUM IN ETHYLENEDIAMINE

Reaction of friedelan 3 4 olide 1, with lithium in ethylenediamine for 2 hours furnished a single compound which was subjected to column chromatography. On elution with solvents of increasing polarity benzene-chloroform (4:1) mixture gave a solid, compound A

Identification of compound A :-

The compound A was crystallised from chloroform-petrol, *M.P.*173-4^{o}C. Its IR spectrum (fig.1) showed a broad absorption at 3420 cm^{-1} showing the presence of hydroxyl groups indicating thereby that the lactone ring has been reduced into hydroxy groupings. The Mass spectrum (fig.2) showed molecular ion peak at m/e 428 which is due to loss of one molecule of water from the molecular ion $(M-H_2O, 0.2\%)^{+}$; therefore the actual molecular ion peak was to be m/e 446 (M^{+}), other important peaks were found at 413 (4),402 (20), 397 (8), 273 (20),219 (14), 205 (90), 191,163,149,137,123,109,95(100).

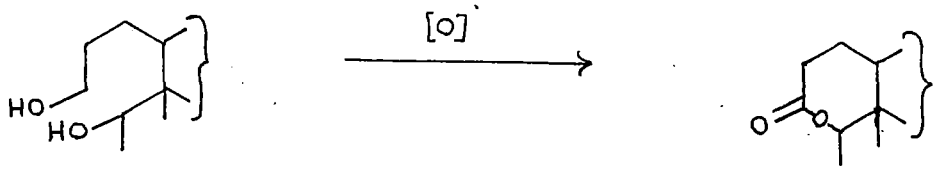
Elemental analysis and mass spectrum suggested the molecular formula to be $C_{30}H_{54}O_2$. The ^{1}H NMR (fig.3) showed the presence of seven tertiary methyl groups as singlets (3H each) between 0.87 to 1.16 ppm. and a doublet at 1.18 ppm with coupling value of 7 Hz. integrated for three protons is due to secondary methyl group at C-4 position; the AB quartet due to methine proton at C-4 probably merged with the multiplet of methylene protons at C-3 giving rise to a multiplet centred at 3.6 ppm. Thus compound A is acertained as 3,4 seco friedelan 3,4 diol-3.



3,

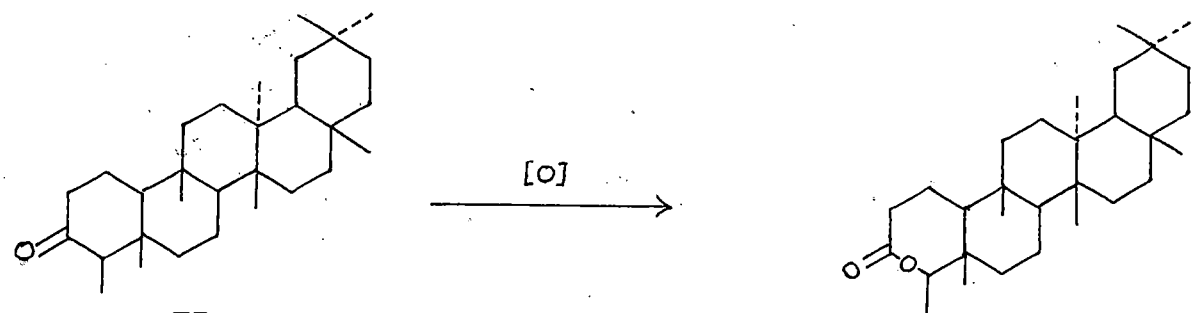
OXIDATION OF 3,4 SECO-FRIEDELAN 3→4-DIOL 3 BY JONES REAGENT.

The compound A when oxidised with Jones reagent gave back the starting material friedelan 3→4 olide 1,as identified by comparison of (m.p., m.m.p. and Co-tlc). This observation shows that the primary hydroxyl group is preferentially oxidised by Jones reagent to the carboxyl group which immediately undergoes lactonisation with less reactive secondary hydroxyl group at C-4 position.

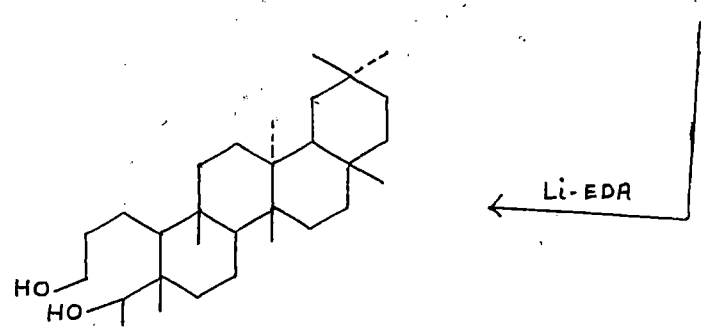


3, 1,

The reaction from friedelin 30 to 3,4 seco friedelin 3,4 diol 3 is schematically shown below :-



30, 1,



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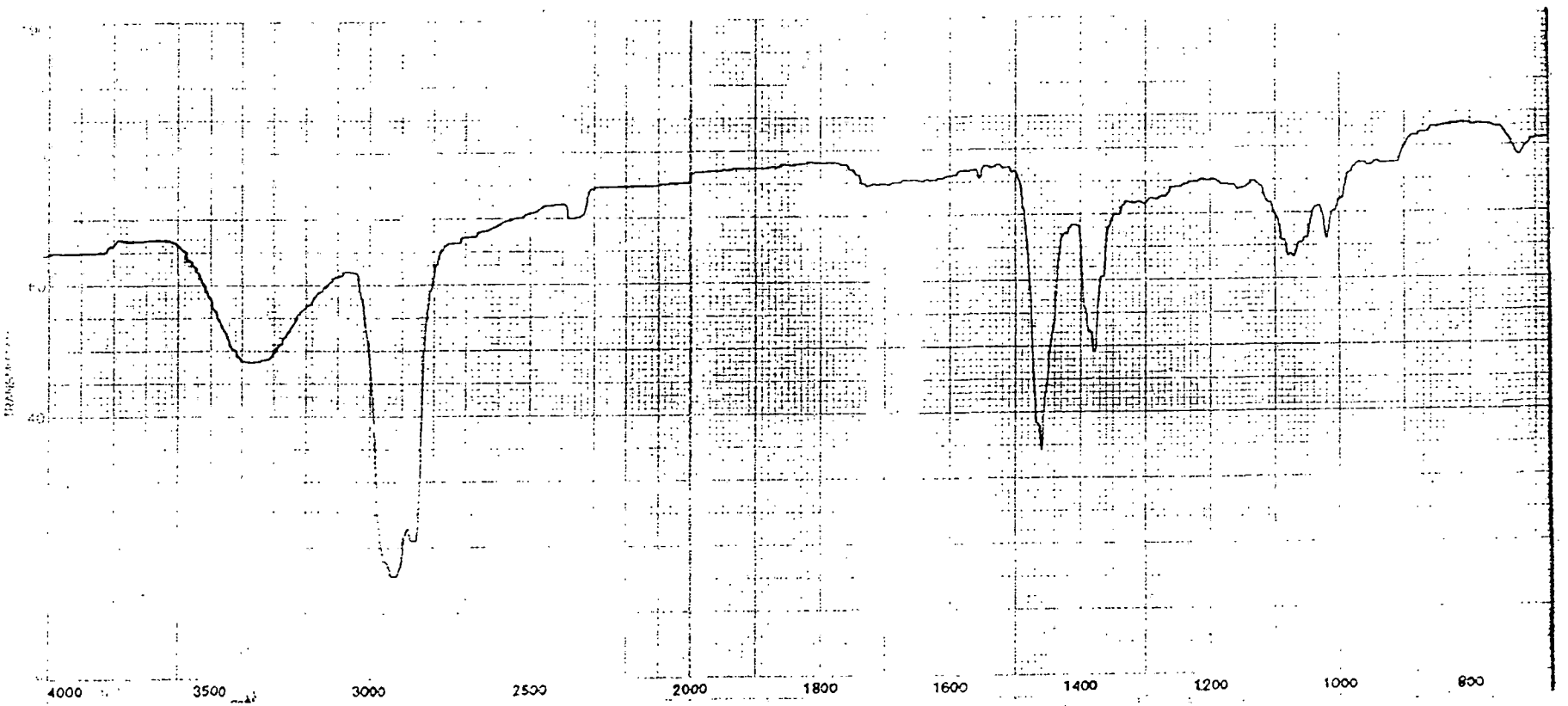


Fig. 1 : IR spectrum of 3,4 seco friedelan 3,4 diol. 3.

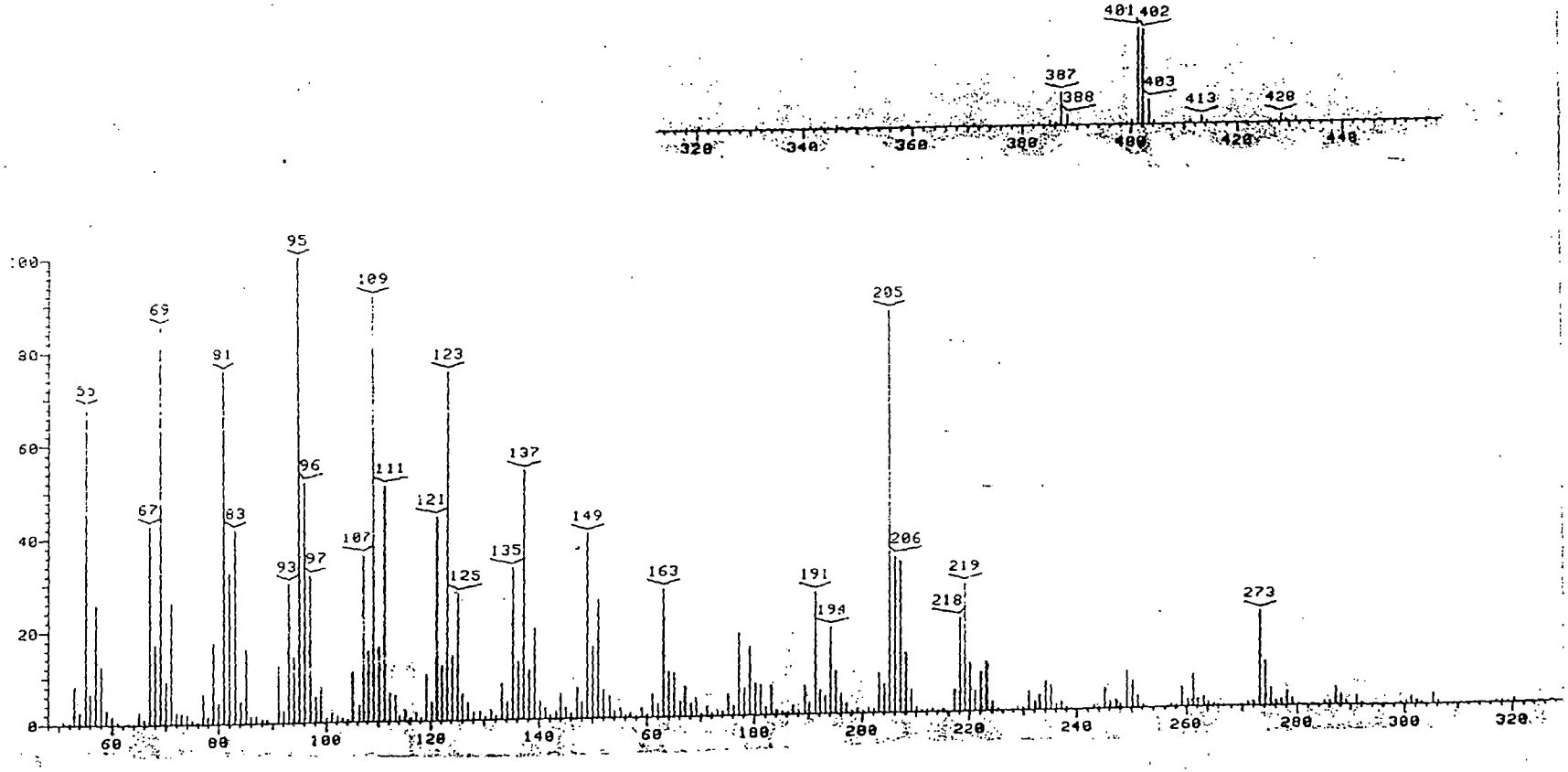


Fig.2. Mass spectrum of 3,4 seco friedelan 3,4-diol, 3.

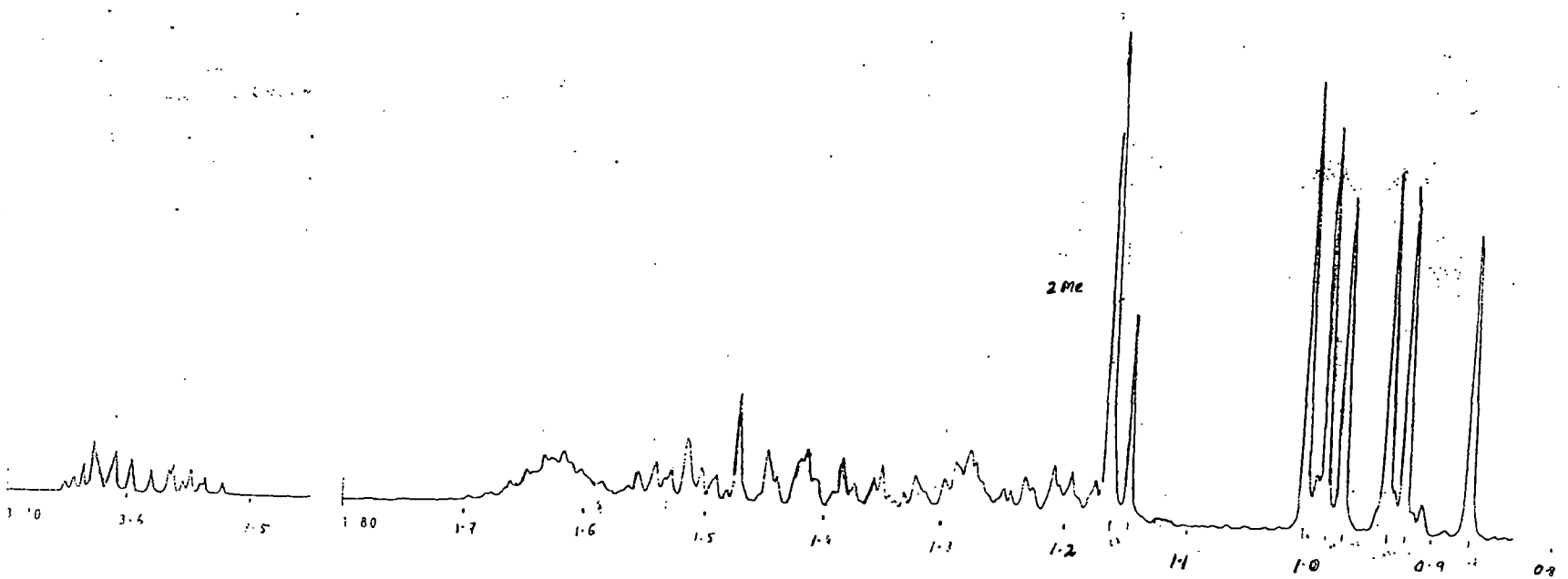


Fig.3. ^{1}H NMR spectrum of 3,4 seco friedelan 3,4 diol, 3.

REDUCTIVE CLEAVAGE OF 3,4 SECO FRIEDELAN 3→4,27→15 DI-OLIDE WITH LITHIUM IN ETHYLENEDIAMINE.

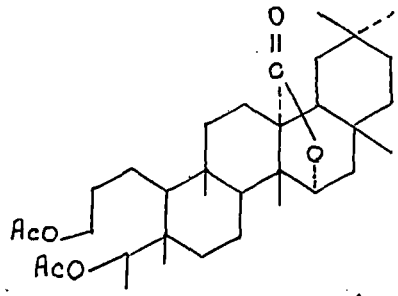
Reduction of friedelan 3→4,27→15 di-olide 2, with lithium ethylene-diamine afforded a single product which was difficult to purify either by crystallisation or column chromatography. As the IR spectrum of the crude reaction product showed the presence of hydroxyl group along with the lactone carbonyl group, it was acetylated with acetic anhydride-pyridine mixture and the product was chromatographed.Elution with benzene-petrol (2:3) a solid material, compound B was obtained.

Characterisation of compound B :

The compound B was crystallised from chloroform-methanol, *M.P.* 241-2°C. Its IR spectrum (fig.4) showed absorption peaks at 1260 due to acetate group and 1750 cm^{-1} (broad) due to merging of lactonic carbonyl peak with acetate carbonyl peak. Mass spectrum (fig.5) showed molecular ion peak at m/e 558 $(M,0.7\%)^+$; other important peaks found were at m/e 514 $(M-CO_2)^+$,498 $(M-AcOH,1.8)^+$,471 (100), 425, 411, 369, 341, 315, 269. From mass and elemental analysis the molecular formula is calculated to be $C_{34}H_{54}O_6$.

The ^1H NMR (fig.6)showed (δ in ppm.) six singlets between 0.83 to 1.16 and one doublet centred at 1.14 (J= 7Hz.) which are accounted for seven methyl groups of which one at C-4 that coupled with the geminal methine proton giving rise to the doublet observed; two sharp singlets (3H each) that appeared at 2.02 and 2.05 indicates the presence of two acetate functions; one AB quartet that centred at 4.83 is due to the methine proton at C-4.The multiplet centred at 3.96 is accounted for the methylene protons at C-3 which coupled with the neighbouring protons. The methine proton at C-15 coupled with adjacent protons giving rise to the triplet at 4.34 (J= 3 Hz.).

Hence, from the spectral studies the structure of compound B is proposed to be 3,4 seco friedelan 3,4 dio-acetoxy 27→15 olide 5



5,

The formation of dihydroxy lactone from the dilactone during reduction with lithium-ethylenediamine indicated that the ε-lactone ring at 3→4 is much more exposed to the reagent and the γ-lactone ring at 27→15 is sterically hindered, is well documented from this observation; the parent lactone at 27→15 in odollactone forms acid and small amount of triol.[5]

Mechanism of lactone cleavage :-

The reductive action of lithium in ethylenediamine is stereoselective as evident from this reaction. The ring-A lactone is very much sterically exposed than the lactone at C_{27} — C_{15} which is crowded. Thus there is a strong competition of these two lactones for reaction with the reagent and the lactone at C_3-C_4 undergoes Bouveault Blanc reduction by protonation of the lactone radical-anion concerted with the second electron transfer. This allows the acyl oxygen fission to take place with the formation of alkoxide ion and aldehyde group in the same molecule. Further reduction and protonation of the aldehyde group than affords the diol.

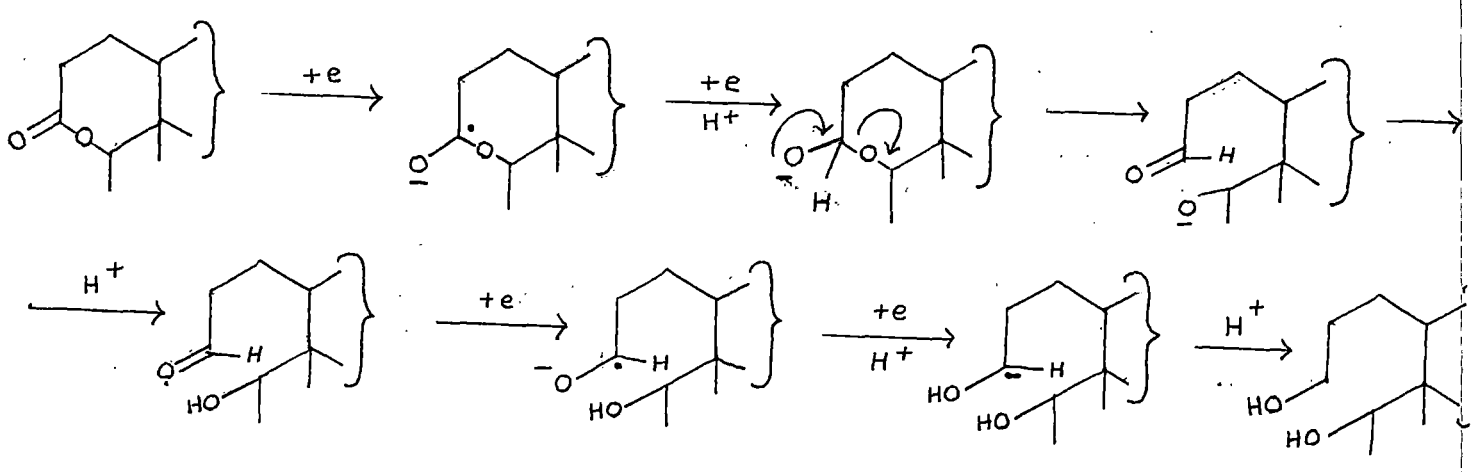


Fig.4. IR spectrum of 3,4 seco 3,4 dio-acetoxy friedelan 27→15-Olide, 5.

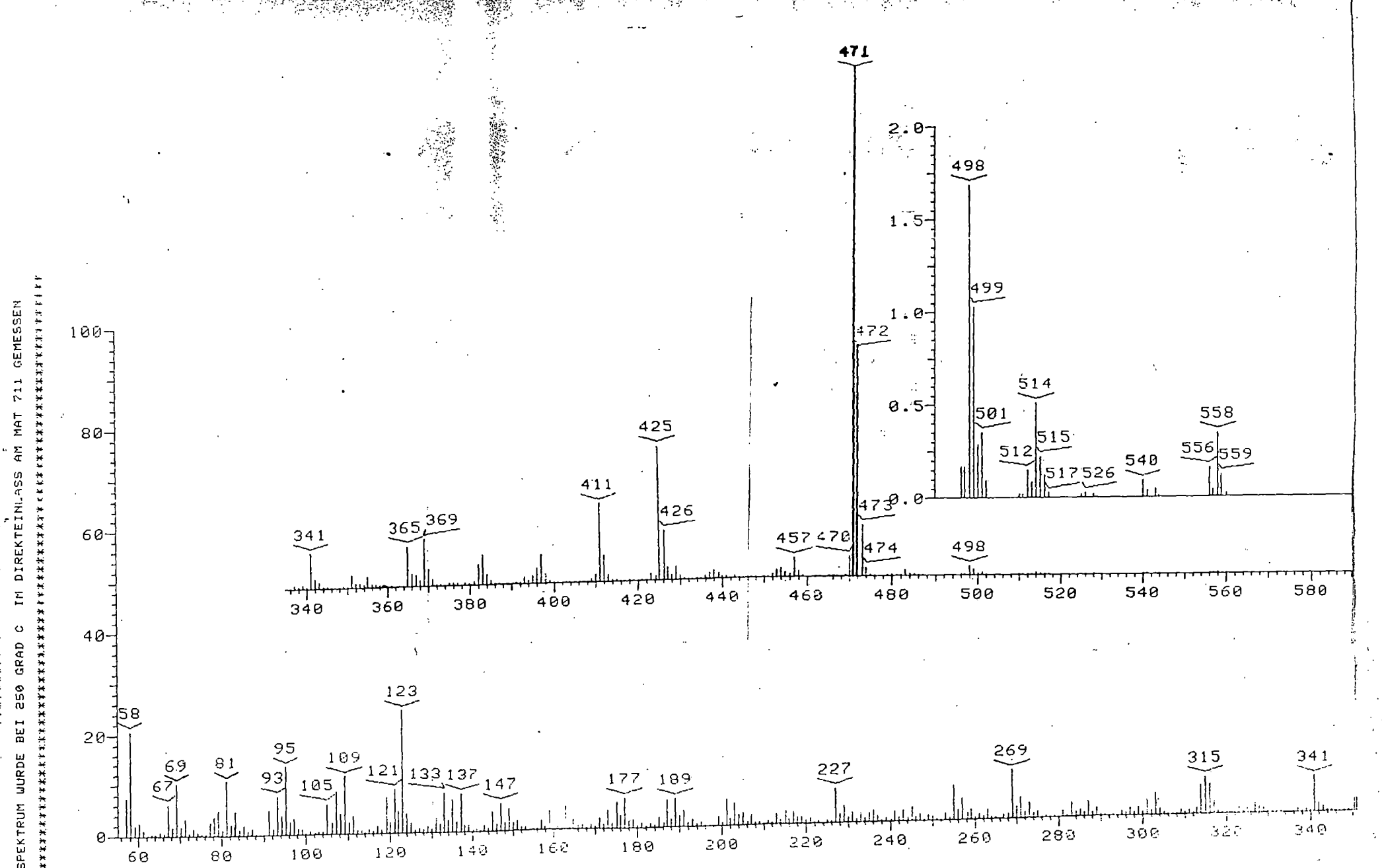


Fig.5. Mass spectrum of 3,4 seco 3,4 dio-acetoxy friedelan 27→15-olide, 5.

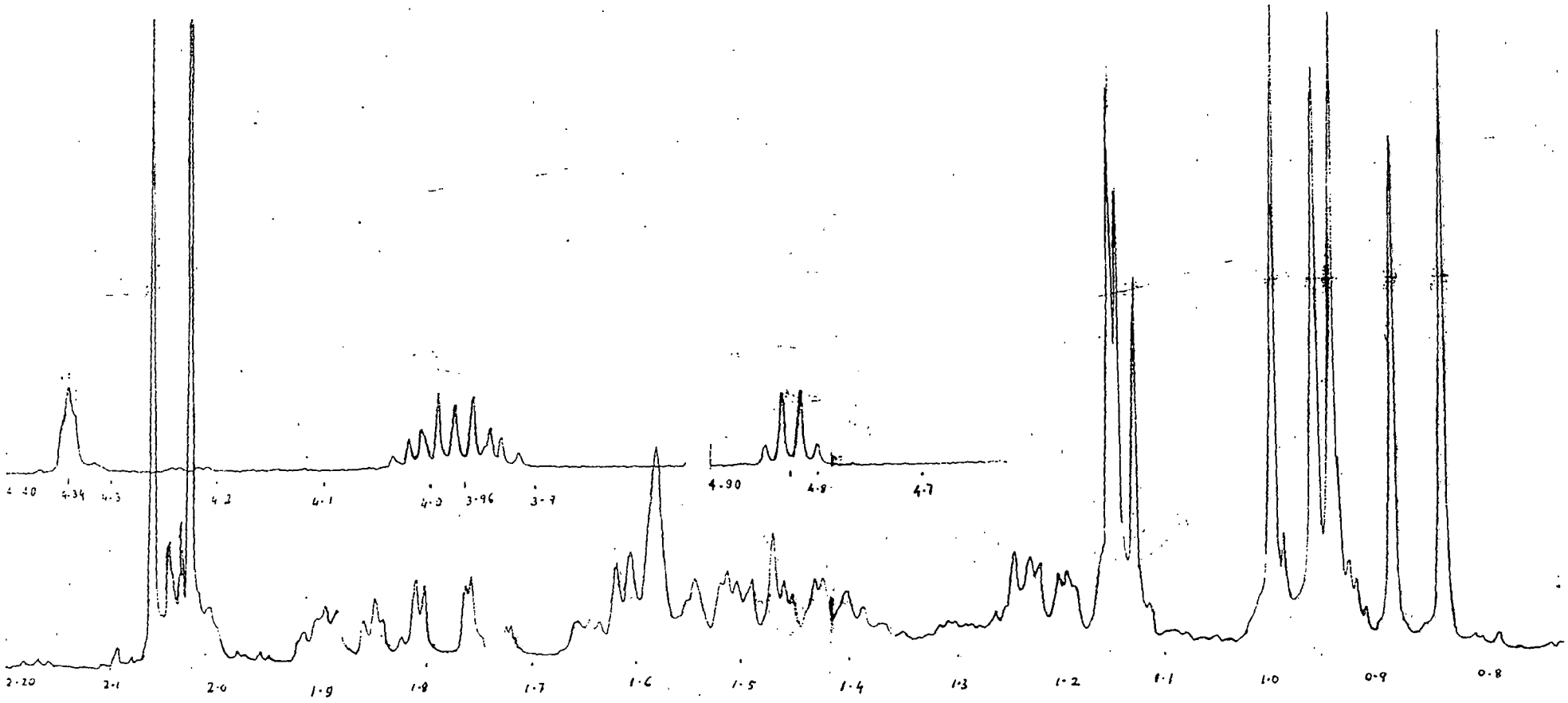


Fig.6. ^{1}H NMR spectrum of 3,4 seco 3,4 dio-acetoxy friedelan 27→15-olide, 5.

OXIDATION OF FRIEDELIN 30, TO FRIEDELAN 3→4 OLIDE 32 BY META CHLORO-PERBENZOIC ACID.

This method has been discussed in the experimental section of part-III of this thesis.

REDUCTIVE CLEAVAGE OF FRIEDELIN 3→4 OLIDE 1 WITH LITHIUM ETHYLENE-DIAMINE.

About 1.0 g of compound 1 was dissolved in 150 ml.of dry ethylenediamine and lithium metal 1.0 g was added in small pieces at intervals. The mixture was than refluxed over heating mentle for 2 hours and it was allowed to cool. Then excess lithium metal was destroyed by adding solid NH_4Cl and acidified with (1:1) HCl. The compound was then extracted with ether, washed with water till neutral and ether layer was dried with anhydrous Na_2SO_4. Finally the solvent was distilled off to yield a gummy mass (0.6 g) which was chromatographed over silica gel column.

TABLE-I

Eluent	Fraction of 50 ml each.	Residue on distillation.
1. petrol	1-3	nil.
2. petrol-benzene (4:1)	4-6	nil.
3. petrol-benzene (3:2)	7-10	nil.
4. petrol-benzene (1:4)	11-13	nil.
5. benzene	14-16	nil.
6. benzene-chloroform	17-22	solid (0.6)

further elution did not afford any compound more.
The fractions 17-22 were collected together and crystallised from $CHCl_3$-petrol, *M.P.*173-4^oC. identified as 3,4 seco friedelan 3,4 diol 3.

ANALYSIS REPORT.

Found :	C 79.6 H 9.8%
Calculated for $C_{30}H_{54}O_2$:	C 80.7 H 10.2%
IR (nujol) : ν_{max}	3350 cm^{-1}. (broad) (2X-OH)
	fig.1
Mass : m/e	446 (M^+), 428, 413, 402, 397, 273, 219, 205, 191, 163, 123, 109, 95 (100).
	fig.2
^1H NMR ($CDCl_3$) : (δ in ppm.)	0.87, 0.92, 0.94, 0.97, 0.96 1.05, 1.15 (7s.21H,7Xt-CH_3)
	1.18 (d, J= 7 Hz. -C_4H-CH_3)
	3.6 (m,2H+1H,-CH_2-OH,-CH-OH)
	fig.3

OXIDATION OF SECO FRIEDELIN 3,4 DIOL 3 BY JONES REAGENT.

0.2 g of compound 3 was dissolved in acetone (20 ml.) and Jones reagent was added dropwise with constant shaking till a orange colour persisted. The mixture was then kept at room temperature for 1 hour and diluted with water when a white solid mass separated out, which was filtered using suction, washed with water and finally dried.

It was crystallised from $CHCl_3$-MeOH, *M.P.*273-4°C, found to be identical with friedelan 3→4 olide 1.

OXIDATION OF FRIEDELAN 3-OXO,27→15 OLIDE TO FRIEDELAN 3→4, 27→15 DI-OLIDE BY META CHLOROPERBENZOIC ACID IN CHLOROFORM.

This step is discussed in the experimental portion of part-III of this thesis.

REDUCTIVE CLEAVAGE OF FRIEDELAN 3→4, 27→15 DI-OLIDE WITH LITHIUM ETHYLENEDIAMINE.

The compound 2 (1.0 g) was dissolved in dry ethylenediamine and 1.0 g of lithium metal was added in small pieces at intervals. The mixture was stirred with a magnetic stirrer for 3 hours at room

temperature and after the reaction solid NH_4Cl was added to destroy excess Li-metal. The mixture was than cooled, acidified with (1:1) HCl and extracted with ether, washed with water, dried with anhydrous Na_2SO_4 and finally the solvent was distilled off to give a gummy mass (0.6 g) which was difficult to purify by chromatography. As the IR spectrum indicated absorption in the region 3200-3600 cm^{-1}.it was than acetylated with acetic anhydride-pyridine mixture. The acetylated product was than chromatographed with solvents as shown in table-II.

TABLE-II

Eluent	Fraction of 50 ml each.	Residue on distillation
1.petrol	1-5	nil
2.petrol-benzene (1:4)	6-10	nil
3.petrol-benzene (2:3)	11-15	solid, (0.7 g)

The fractions 11-15 were crystallised from $CHCl_3$-MeOH to furnish white crystalline compound identified as seco friedelan 3,4 dio-acetoxy-27→15 olide **4** , *M.P.* 241-42°*C*.

ANALYSIS REPORT.

Found : C 72.40 ; H 10.36%

Calculated for $C_{34}H_{54}O_6$: C 72.56 ; H 10.37%

IR (nujol) : ν_{max} 1260 and 1750 cm^{-1}.
(-CO-, $-CH_3$-CO-O-)
fig.4

Mass : m/e 558 (M^+),514, 498, 471 (100)
425, 411, 369, 341, 315, 269.
fig.5

^1H NMR ($CDCl_3$) : (δ in ppm.)
0.84, 0.86, 0.94, 0.96, 1.00
1.16 (7s,21H,7Xt-CH_3)
1.14 (d,J= 7 Hz.-C_4H-CH_3)
2.02 and 2.05
(2s,6H,2X-O-CO-CH_3)
3.96 (m,-CH_2-OAc)
4.34 (t,1H,-CO-O-CH-)
4.83 (AB_q,1H,-C_4H-CH_3) fig.6

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Studies on the reactions of N-bromosuccinimide in dimethyl sulfoxide: Part IV—Action on lupenyl acetate

B P Pradhan*, D K Chakraborty†, S Dutta, R Ghosh‡ & A Roy
Department of Chemistry, University of North Bengal, P.O. North Bengal University, Darjeeling 734 430

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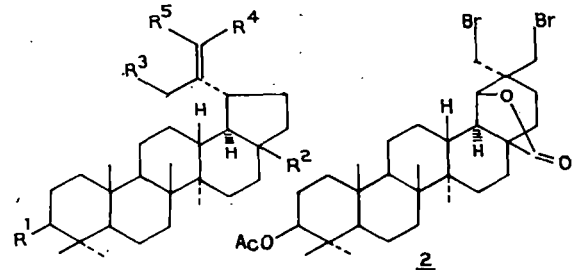
Action of N-bromosuccinimide on lupenyl acetate (**1**) in dimethyl sulfoxide has been studied. The compounds so formed have been identified as 30-bromolupenyl acetate (**1a**), 29-(*E*-*Z*)-bromolupenyl acetates (**1c** and **1d**), and 29,30-dibromo-18-iso-oleanan-19α-hydroxy 3β-yl acetate (**3a**). Further treatment of **1a** and mixture of **1c** and **1d** with NBS in DMSO containing water afforded 30-oxo-lupeol (**1k**) and 20-(*E*-*Z*)-bromo-lupeol (**1l** and **1m**) respectively; compound **1a** on alumina column afforded 30-hydroxylupenyl acetate (**1h**) and 30-hydroxylupeol (**1i**).

The action of N-bromosuccinimide (NBS) in CCl_4 on lupenyl acetate has been studied by Ramachandra Rao *et al.*[1] who have reported the isolation of 30-bromolupenyl acetate (**1a**) as the reaction product. The action of NBS in dimethyl sulfoxide (DMSO) on methyl acetylbetulenate (**1b**) has been reported from our laboratory[2], and the isolation of rearranged dibromolactone (**2**) prompted us to explore the applicability of the reaction on lupenyl acetate (**1**). Lupenyl acetate in chloroform when treated with NBS in DMSO furnished the compounds A, B and C (see Experimental). The compounds A and B on oxidation with NBS in DMSO in the presence of water yielded compounds F and G. The hydrolysis of A on alumina column furnishing compounds H and I has also been studied. Determination of structures of all the compounds (A-I) was fully corroborated by chemical and spectral studies. From IR and PMR spectral data (see Experimental) the compound A was characterised as 30-bromolup-20(29)-en-3β-yl-acetate (**1a**)[1].

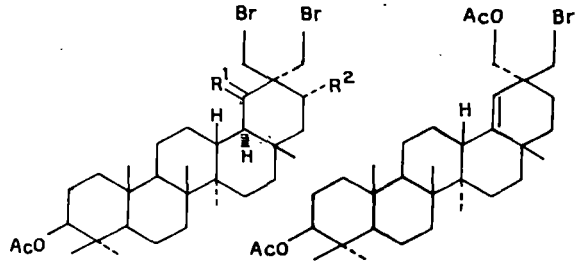
Compound B in its PMR spectrum showed two pairs of singlets at δ 1.71 and 1.72 and 5.72 and 5.90 which integrated for three protons and one proton respectively and were attributed to the presence of E and Z isomers arising out of the C-20(29) olefinic group with bromine atom with it. Thus the product 29-bromolupenylacetate[3] is a mixture of 29-*E*-bromo (**1c**) and 29-*Z*-bromo (**1d**) lup-20(29)-en-3β-yl-acetate.

Similarly 29-*E* and *Z*-bromomethylacetyl betule-



2

1, R^1 = OAc, R^2 = CH_3, R^3 = R^4 = R^5 = H
1a, R^1 = OAc, R^2 = CH_3, R^3 = Br, R^4 = R^5 = H
1b, R^1 = OAc, R^2 = COOMe, R^3 = R^4 = R^5 = H
1c, R^1 = OAc, R^2 = CH_3, R^3 = R^5 = H, R^4 = Br
1d, R^1 = OAc, R^2 = CH_3, R^3 = R^4 = H, R^5 = Br
1e, R^1 = OAc, R^2 = COOMe, R^3 = R^5 = H, R^4 = Br
1f, R^1 = OAc, R^2 = COOMe, R^3 = R^4 = H, R^5 = Br
1g, R^1 = R^3 = OAc, R^2 = CH_3, R^4 = Br, R^5 = H
1h, R^1 = OAc, R^2 = CH_3, R^3 = OH, R^4 = R^5 = H
1i, R^1 = R^3 = OH, R^2 = CH_3, R^4 = R^5 = H
1j, R^1 = R^3 = OAc, R^2 = CH_3, R^4 = R^5 = H
1k, R^1 = OH, R^2 = CH_3, R^3 = O, R^4 = R^5 = H
1l, R^1 = OH, R^2 = CH_3, R_3 = R^4 = H, R^5 = Br
1m, R^1 = OH, R^2 = CH_3, R_3 = R^5 = H, R^4 = Br
1n, R^1 = OAc, R^2 = CH_3, R^3 = O, R^4 = R^5 = H



4

3, R^1 = H_2, R^2 = OH
3a, R^1 = =O, R^2 = H
3b, R^1 = O, R^2 = H
3c, R^1 = H, OH, R^2 = H

†Present address: Central Drug Laboratory, 3 Kyed Street, Calcutta 700 016
‡Present address: Chemistry Department, Dinhata College, Cooch Behar

nates [**1e** and **1f**] crystallised from $CHCl_3$-MeOH analysed for $C_{33}H_{51}O_4Br$, m.p. 228-30°; IR 1735, 1725, 1240, 900 cm^{-1}; PMR: δ 0.78-1.0 (15H, 5t-CH_3), 1.71 and 1.78 (*s*, 3H, C=C-CH_3), 2.05 (*s*, 3H, O-COCH_3), 3.65 and 3.70 (*s*, 3H, -COOCH_3), 4.45 (*m*, 1H, *H*-C-3-O-CO-), 5.76 and 5.97 (*s*, 1H, C=C(Br)H) were isolated (not reported earlier[2]) as the products of the reaction of NBS/DMSO with **1b**.

The most polar product C was purified by crystallisations from $CHCl_3$-MeOH. Its PMR spectrum showed the presence of six tertiary methyls (δ 0.84,0.85, 0.87, 0.89, 0.95 and 1.06) and acetoxy group (δ 2.04) and exhibited two *AB* quartets centered at δ 3.64 (J = 16 Hz) and 3.02 (J = 10 Hz) due to four protons of the two $-CH_2Br$ groups, a one proton doublet of a doublet centered at δ 4.05 (J = 6 and 12 Hz) suggested the presence of a CH bearing a hydroxyl group as evident from the IR band (3330 cm^{-1}). The high J value indicated the hydroxyl to be axially oriented. Such a situation is satisfied if a lupane skeleton rearranges to oleanane skeleton with the hydroxyl group being situated at C-21 for which the structure **3** could be proposed. ^{13}C NMR data could also be accounted for the structure **3**.

Though structure **3** was initially suggested, one of the alternative structures **3a** and **3c** was also highly desired on mechanistic ground. In order to decide amongst the three structures possible **3**, **3a** and **3c**, the following experiments were performed.

Compound C was oxidised with CrO_3-Py in usual manner giving the product D which crystallised from $CHCl_3$-MeOH and analysed for $C_{32}H_{50}O_3Br_2$ m.p. 248-49°. Its IR spectrum showed the absence of hydroxyl band but gave a new band at 1705 beside the acetoxy carbonyl absorption at 1725 and 1245 cm^{-1}. The mass spectrum of D gave peaks at *m/z* 584, 582, 580 in the ratio 1:2:1 indicating the presence of two bromine atoms in the molecule. The peaks could arise by the loss of acetic acid molecule (60 mass units) from the molecular ions which did not appear in the spectrum. The PMR spectrum of D furnished a convincing proof for the structure **3b**. It showed peaks at δ 0.62, 0.75, 0.78, 0.88, 0.94 for the six tertiary methyls, a singlet at 1.94 for the methyl protons of acetoxy group, a one proton doublet at 2.45 with the coupling constant of 12.5 Hz showing that this proton coupled with a single proton which must be *trans* di-axial further indicating that the newly formed carbonyl group has only one neighbouring proton. This suggested the carbonyl group to be at C-19 that has an α-proton as C-18 α-H couples with C-13 β-H. Thus, structure **3a** was assigned for C. The structure of D as **3b** suggested the compound C to be 29,30-di-bromo-19-hydroxyl-18-iso-oleanan-3β-yl-acetate.

The compound C on acetylation furnished compound E which analysed for $C_{34}H_{53}O_4Br$, m.p. 180-81°. Its mass spectrum showed its molecular ion-peaks at *m/z* 606 $[M_1]^+$ and 604 $[M_2]^+$. Its PMR spectrum showed the existence of six tertiary methyls in the region δ 0.70-0.95 two acetoxy methyls at 1.94 and 2.02 a proton at C-3 geminal to acetoxyl group at its usual position of 4.45, a two proton *AB* quartet at 4.65 (J = 14.5 Hz) assignable to the methylene protons geminal to acetoxyl group which must have replaced one of the bromine atoms, and a one proton downfield singlet at 6.1 assignable to an isolated olefinic proton.

The isolated olefinic proton (6.1) could be attributed to the C-19 proton of the derivative **4** which could arise by dehydration of hydroxyl group if it is α-oriented as observed in the case of 19α-hydroxyl-18-iso-oleanan derivative[4]. Thus structure **3c** could be assigned to compound C. However, structure **3c** was rejected on the basis of the fact that E showed the absence of second pair of methylene protons carrying the bromine atom though it still contained a bromine atom. The downfield appearance of this olefinic proton at 6.1 as a singlet suggested it to be attached to the carbon containing the bromine. Thus, the presence of the grouping C=C(H)Br group was envisaged. This is possible only if compound C rearranges under the reaction condition (Py-Ac_2O) from 18-iso-oleanane to lupane skeleton giving rise E. This transformation further suggested that the hydroxyl group at C-19 is *cis* to the 18α-proton. Such a rearrangement is well documented in literature[4], where the 19α-hydroxy-18α-*H*-oleanan-3β-ol on acetylation furnishes lupenyl acetate. Since identical group and stereochemical factors are involved in the present case (C) the stereochemistry of the isopropenyl group in E is also established to be alpha oriented. Thus, E was identified as 29-bromo-3,30-diacetoxy lup-20(29)-ene (**1g**). Further, since a single sharp singlet for the olefinic proton appears in E, only one isomer (**1g**) appears to be formed due to electronic repulsion of the bromine and acetoxy carbonyl groupings. The above observations led to conclude the structure of C as 29,30-dibromo-oleanan-18α*H*-19α-ol-3β-yl acetate (**3a**). The structure **3a** was further confirmed by comparison

of its ^{13}C NMR spectral data with those of compounds **1** and **2** [Table 1].

Compound **1a** was allowed to be adsorbed over alumina column for 3 days. Elution of the column with pet. ether-benzene (3:2) afforded a compound that crystallised from $CHCl_3$ – MeOH and analysed for $C_{32}H_{52}O_3$ (M^+ 484), m.p. 348-59°, $[\alpha]_D \pm 0°$; IR spectra showed the presence of a hydroxyl (3500), an acetoxyl (1715, 1240) and an olefinic methylene (3040, 1640, 890) groupings, PMR spectra showed the presence of six tertiary methyls in the region δ 0.78-1.03 as six singlets, one acetoxy methyl as a singlet at 2.04, a doublet (J = 8 Hz) of two protons that appeared at 4.025 have been assigned to the methylene carbon (C-30) bearing a hydroxyl group; the methine proton geminal to the C-3 acetoxyl group appeared at the usual position at 4.48; the C-29 methylene protons appeared as multiplet at 4.90. Thus on the basis of spectral data this compound was assigned the structure as 30-hydroxy-lupenyl acetate (**1h**).

Table 1—Carbon-13 NMR spectral data (δ, ppm) of **1** (lupenyl acetate)[8], **2** and **3a**

Carbon	**1**[8]	**2**	**3a**
1	38.3	38.6	38.3
2	23.6	23.7	23.6
3	80.7	80.9	80.9
4	37.7	37.7	37.7
5	55.3	55.6	55.2
6	18.2	18.1	18.2
7	34.1	33.7	34.1
8	40.7	41.3	41.2
9	50.2	46.7	49.4
10	37.0	36.4	36.33
11	20.9	21.3	21.2
12	25.0	26.9	25.0
13	37.9	37.8	37.8
14	42.7	40.6	42.8
15	27.4	28.3	28.3
16	35.5	36.6	36.5
17	42.9	51.1	44.4
18	48.2	45.7	45.6
19	47.9	80.8	73.9
20	150.5	35.3	36.9
21	29.8	29.7	26.4
22	39.9	31.1	37.6
23	27.9	27.9	27.9
24	16.5	16.6	16.5
25	16.1	16.5	16.1
26	15.9	15.5	16.0
27	14.4	13.6	14.4
28	18.0	178.0	18.3
29	109.2	39.7	38.6
30	19.2	40.0	43.0

Note: ^{13}C NMR data of **2** not reported in earlier paper[2]

The most polar fraction eluted by benzene-ethyl-acetate (9:1) and crystallised from $CHCl_3$ – MeOH was analysed for $C_{30}H_{50}O_2$, m.p. 235-36°C MS: 442 $[M]^+$; its IR spectrum showed the presence of two hydroxyl groups (3330, 3500) and the olefinic methylene double bond (3040, 1640, 890). The PMR spectrum exhibited signals at (δ): 0.77-1.07 (6*s*, 18H, 6x-t-CH_3), 4.15 (*d*, 2H, $-CH_2OH$, J = 6 Hz), 3.18 (*m*, 1H, HO – C_3H), 4.9 (*m*, 2H, C = CH_2). From these spectral data the compound was identified as lup-20(29)-ene-3β,30-diol[7] (**1i**). Acetylation of **1h** and **1i** with Ac_2O – Py separately furnished the same compound $C_{34}H_{54}O_4$, m.p. 164-65°, M^+ 526; IR 1745, 1730, 1245, 1240 cm^{-1}, identical with 3β,30-diacetoxylup-20(29)-ene (**1g**). Similar adsorption of compound B gave back the starting material (B).

A mixture of A and B was further treated with NBS in DMSO containing 5% water and kept in dark for 25 days. The mixture after usual work-up and chromatography over silica gel furnished two compounds (F and G). Compound F was analysed for $C_{30}H_{49}OBr$ (M^+ 514) m.p. 174-75°, gave positive test for halogen (Beilstein test) and unsaturation (TNM); its IR spectrum showed the presence of hydroxyl group (3400 cm^{-1}) and tri-substituted double bond (910 cm^{-1}). It was identified as 29-bromo-lupeol (**1l** and **1m**) by acetylation to B. Acetylation of F with Py – Ac_2O afforded an acetate $C_{32}H_{51}O_2Br$, m.p. 185-6°, identical with B. The second compound (G) was crystallised from $CHCl_3$ – MeOH. It analysed for $C_{30}H_{50}O_2$ m.p. 234-35°C, MS: 440 $[M]^+$; UV 228 nm and IR 1690, 1630 (α,β-unsaturated carbonyl group), the peak at 3320 cm^{-1} (OH); did not respond to Beilstein test for halogen but gave yellow colouration with TNM. It was identified as 30-oxolupeol (**1k**). Its acetate was identical with 30-oxo-lupenyl acetate[7] (**1n**).

The formation of **1a** and a mixture of **1c** and **1d** indicated that with NBS in polar solvent both allylic bromination by free radical mechanism and bromonium ion attack takes place with equal ease at the isopropyl group of lupane skeleton. In case of methyl acetyl betulenate (**1b**) the bromonium ion attack gives rise to the lactone **2** when the lactonic oxygen is β-oriented at C-19 whereas the lupenyl acetate (**1**) the ring expansion is accompanied by hydroxylation at C-19 but its orientation is alpha. It is to be noted that the stereochemistry of C-18 proton remains intact as alpha showing that no olefinic double bond is formed to give the germanicene type skeleton (**4**) before lactonisation in the case of **1b**[2] or hydroxyla-

tion in the case of **1**. Further, since only the dibromo compounds give rise to the oleanane derivatives, it may be suggested that a small amount of bromonium ion may attack the olefinic bond in two different ways; in isopropyl derivative the three membered ring bromonium ion can open up with the loss of a proton from the C-29 give **1c** + **1d**/**1e** + **1f** from **1**/**1b** whereas the isopropyl group with allylic bromine at C-30 opens up in a different manner giving rise to a cation at C-20 or may undergo simultaneous ring expansion and addition to furnish **3a**/**2**.

The formation of **1h** during column chromatography showed that the bromine on sp^3 carbon undergoes facile hydrolysis than the 3-acetate, whereas the aqueous NBS causes allylic bromination, hydrolysis and oxidation to yield the allylic aldehyde **1k**.

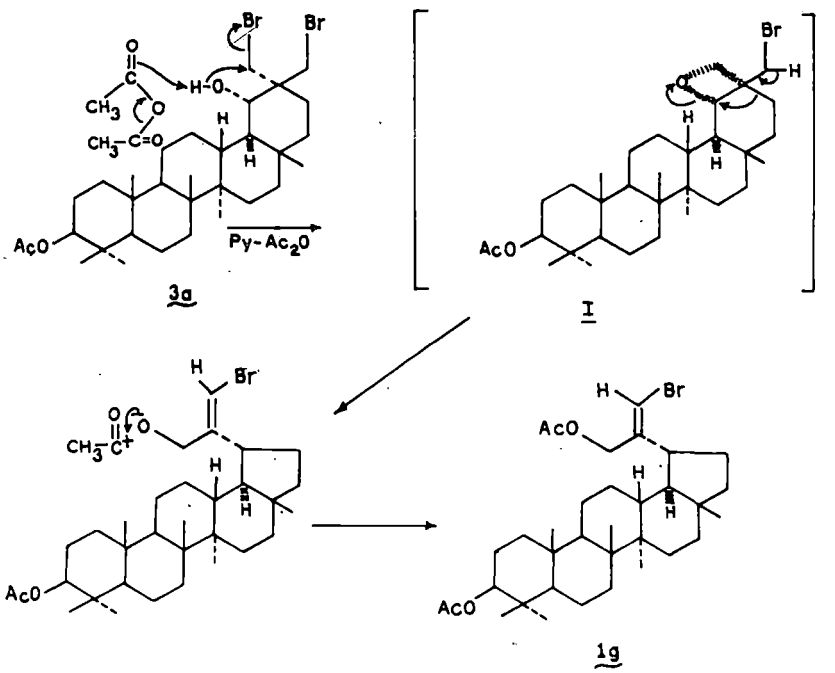
The rearrangement of **3a** to **1g** during acetylation is almost similar to the previous observation[4] (where acetylation of 3β,19α-dihydroxy-18α-H-oleanane-yielded lupenyl acetate). It has been observed that 30-bromolupenyl acetate (**1a**) when treated with Ac_2O – Py under usual acetylation conditions no 30-acetoxylupenyl acetate (**1j**) was formed showing that the bromine at C-30 in **1a** is unreactive with Ac_2O – Py. Under acetylation conditions the hydroxyl oxygen being at a closer proximity to the C-30 bromine and bromine being a better leaving group a nucleophillic attack takes place with the liberation of bromide ion to give an unstable four membered ring **I**. This immediately undergoes E-ring contraction with opening of the oxo-ring giving rise to **1g**.

Experimental Procedure

Melting points are uncorrected. The pet. ether used had b.p. 60-80°. Alumina (S. Merck) deactivated with 5% or 10% AcOH was used for column chromatography. TLC plates were coated with silica gel G and the spots located by exposing to iodine vapours. All optical rotations were determined in chloroform. IR spectra were recorded as nujol mulls on a Beckmann IR-20 spectrophotometer, UV spectra in MeOH on a Beckmann DU-2 spectrophotometer, PMR spectra in $CDCl_3$ on Varian A-60 or T-60 or EM-360 spectrometer. ^{13}C NMR spectra in $CDCl_3$ on an FT-80A instrument using TMS as internal standard. Mass spectra were recorded by solid probe C1/CH4 method.

Treatment of Lupenyl acetate with NBS in Dimethyl Sulfoxide: Formation of 30-bromo-lup-20(29)-en-3β-yl acetate (**1a**), *29(E-Z)-bromo-lup-20(29)-en-3β-yl-acetate* (**1c** *and* **1d**) *and 29,30-di-bromo oleanan-18α-H-19α-ol-3β-yl acetate* (**3a**)

To a solution of lupenyl acetate (1 g) in $CHCl_3$ (10 ml) and DMSO (25 ml), crystals of NBS (1 g) were added in lots of 100 mg each with constant shaking and the solution was kept in dark for 24 hr. The mixture was diluted with water, the $CHCl_3$ layer washed, dried and concentrated to give a residue (900 mg) which was chromatographed over alumina column. Elution with solvents of increasing polarity furnished compounds A (500 mg, pet. ether benzene) 4:1), B (200 mg, pet. ether benzene 3:2) and C (160 mg, benzene-chloroform 9:1).



Compound A: 30-*Bromo lupenyl acetate* (**1a**)

It was crystallised from $CHCl_3$–MeOH, m.p. 236-37° [Lit[1] m.p. 235-36°] $[\alpha]_D$ +12°, gave Beilstein test positive, IR 1725, 1255 ($OCOCH_3$) 3015, 1640 and 880 cm^{-1} (C=CH_2); PMR: δ0.79, 0.83, 0.84, 0.85, 0.95,1.02 (6*s*, 6×t-CH_3), 2.04 (*s*, 3H, $OCOCH_3$), 3.99 (*s*, 2H, CH_2Br), 4.48 (*m*, 1H, AcO–C_3–*H*), 5.04, 5.12 (2*s*, 2H, C=CH_2) (Found: C, 70.12; H, 9.3. Calc. for $C_{32}H_{51}O_2Br$: C, 70.2; H, 9.3%).

Compound B: 29(*E-Z*)-*Bromolupenyl acetate* (**1c** *and* **1d**)

It was crystallised four times from $CHCl_3$–MeOH m.p. 186-88°, $[\alpha]_D$ +32°; IR: 1735, 1240 ($OCOCH_3$) and 1265 cm^{-1} (=CHBr); MS: m/z 548, 546 (M^+), 467, 407, 203, 189, 109 (base); PMR: δ 0.79, 0.84, 0.85, 0.86, 0.92, 1.02 (6*s*, 18H, 6×t–Me), 1.71 and 1.73 (*s*, 3H, =C–CH_3), 2.05 (*s*, $OCOCH_3$), 4.48 (*m*, 1H, AcO–C_3–αH), 5.72, 5.91 (2*s*, 1H, C_{29}–H), identical (m.m.p., co-TLC) with an authentic sample of 29-bromolupenyl acetate (**1c**) and (**1d**).

Compound C: 29,30-*Dibromo*-19α-*hydroxy*-18α*H*,3β-*yl acetate* (**3a**)

It was crystallised from $CHCl_3$–MeOH, m.p. 258-60°; TNM test: negative; Beilstein test tor halogen: positive; IR: 3330 (–OH) 1732 and 1250 ($OCOCH_3$) cm^{-1}; MS[+]: ** 646 [M_1, 1%]**, 644 [M_3, 2%]+, 642 [M_2, 1%]+, 626 [M_1–HBr, 2%]+, 624 [M_3–HBr]+, 622 [M_2–HBr, 2%]+, 586, 584, 582 [M–HOAc, 1:2:1, 5%], 565, 564, 563, 562 [M–HBr, 5%], 547 (4%), 531 (2%), 505, 504, 503, 501 (5%), 483 (20%), 466 (7%), 452 (3%), 423 (10%), 313 (4%), 297 (5%), 283 (5%), 269 (4%), 249 (6%), 204 (15%), 189 (100%); PMR: δ 0.84, 0.85, 0.87, 0.89, 0.95, 1.06 (6*s*, 6×t-CH_3), 2.04 (*s*, 3H, $OCOCH_3$), 3.64 (*ABq*, 2H, CH_2–Br, J=16 Hz), 3.02 (*ABq*, 2H, –CH_2Br, J=10 Hz), 4.05 (*dd*, 1H, HO–$C_{19}\beta$–H, J=6 and 12 Hz), 4.45 (*m*, 1H, AcO–$C_3\alpha$–H) (Found: C, 59.6; H, 8.05. $C_{32}H_{52}O_3Br_2$ requires C,59.6; H, 8.1%).

Oxidation of **3c**: 29,30-*Dibromo-oleanan*-18α*H*-19-*one* (**3b**)

Compound C (0.1 g) dissolved in pyridine (1 ml) was mixed with CrO_3 (0.1 g) in pyridine (1 ml) in cold. After usual work-up and purification of the product by chromatography and crystallisations furnished crystals of **3b**, m.p. 248-49°, IR: 1725, 1245 ($OCOCH_3$) and 1705 cm^{-1} (CO); MS (*m/z*): 584 [M_1–AcOH]+, 582 [M_3–AcOH]+, 580 [M_2–AcOH]+, 569, 567, 565, 503, 502, 501, 475, 474, 473, 393, 391, 191, 189, PMR: δ 0.6, 0.75, 0.78, 0.88, 0.94 (6*s*, 6×t-CH_3), 1.94 (*s*, $OCOCH_3$), 2.45 (*d*, 1H, 18αH, J=12.5 Hz), 3.46 and 3.82 (dd, 2H, –CH_2Br, J=465; 12, 2 Hz) 3.67 and 3.81 (dd, 2H, CH_2Br, J=195, 12 Hz), 4.39 (*m*, H, C_3–αH), (Found: C, 59.6; H, 7.8; $C_{32}H_{50}O_3Br_2$, requires C, 59.63; H, 7.8%).

Acetylation of compound C

Compound C (0.1 g) dissolved in Py (1 ml) was mixed with Ac_2O (1 ml) and the mixture kept on a water bath overnight. Usual work-up and chromatography followed by crystallisation furnished the acetate E (0.1 g), m.p. 180-81°, IR: 1730, 1725, 1250, 1245 (2×$OCOCH_3$), 3015, 1640 and 840 cm^{-1} (>C=C<H); MS [*m/z*] 606, 604 [M^+], 546, 544, 466, 465, 406, 405, 189; PMR: δ 0.70, 0.76, 0.78, 0.79, 0.81, 0.96 (6*s*, 6×t-CH_3), 1.94, 2.02 (2*s*, 2×–$OCOCH_3$), 4.45 (*m*, 1H, C_3–αH), 4.65 (*ABq*, 2H, CH_2OAc), 6.10 (*s*, 1H, =C*H*Br), identified as 29-bromo-3β,30-diacetoxy-lup-20(29)-ene (**1g**).

Treatment of compound A and B with NBS in DMSO containing water. Isolation of compounds **1l**, **1m** *and* **1k**

To a mixture of compounds A and B (500 mg) in $CHCl_3$ (12 ml), DMSO (12.5 ml), crystals of NBS (500 mg) were added with constant shaking followed by water (2 ml). The mixture was kept in dark for 25 days and diluted with water, extracted with $CHCl_3$ and washed with water, dried and concentrated to give yellow residue (425 mg) which was chromatographed over silica gel. Elution with solvents of increasing polarity gave compounds **1l** and **1m** (200 mg). These were crystallised from $CHCl_3$–MeOH, m.p. 174-75°, TNM test: positive and Beilstein test: positive. IR 3400 (–OH) and 910 cm^{-1} (>C=C<H), MS: (*m/z*) 506 [M_1]+, 504 [M_2]+, 425, 408, 407, 207, 203; PMR: δ 0.75, 0.81, 0.82, 0.91, 0.95, 1.01 (6*s*, 6×t-CH_3), 1.71 (*s*, 3H, C=C–CH_3), 3.2 (*m*, H, C_3–αH), 5.89 (C=C*H*Br) (Found: C, 71.2; H, 9.8. Requires C, 71.3; H, 9.8%). The identity of these compounds was further confirmed by preparing its acetate, which was identical with compound B. m.p. and m.m.p. 185-86°C.

*M_1^+ represents molecular mass due to bromine 81, M_2^+ due to bromine 79 and M_3^+ due to bromine of isotropic masses 79 and 81 when two bromine atoms are present.

Compound **1k** was crystallised from $CHCl_3-MeOH$ to give crystals m.p. 235-6°, UV 228; IR 3320 ($-OH$), 1690 and 1630 cm^{-1} ($C=C-C=O$), Beilstein test for halogen: negative; TNM test: positive; MS: (*m/z*) 440 $[M]^+$, 422 $[M-H_2O]^+$, 407 $[422-CH_3]^+$, 207, 203, 190, 189; PMR: δ 0.75, 0.81, 0.82, 0.92,0.96, 1.01 (6*s*, 6 × t-CH_3), 3.18 (*m*, 1H, $C_3\alpha H$),5.91 and 6.28 (2*s*, 2H, $-C=CH_2$), 9.51 (*s*, H, $-CHO$). This compound (**1k**) which was identified as 30-oxo lupeol by preparation of its acetate which was identical with 30-oxo-lupenyl acetate (**1n**).

The acetate **1k** (50 mg) was obtained by its treatment with pyridine (2.5 ml) and Ac_2O (2 ml) on a water-bath for 4 hr followed by usual work-up, m.p. 224-26° ($CHCl_3-MeOH$), identical with an authentic sample of 30-oxo-lupenyl acetate (**1n**).

Adsorption of compound A on alumina: Isolation of 30-hydroxy lupenyl acetate (**1h**) *and 30-hydroxy-lupeol* (**1i**)

Compound **1a** (250 mg) in benzene (1 ml) was adsorbed over active alumina column (30 gm) developed with petroleum ether and allowed to stand for 24 hr. Elution with solvents of increasing polarity afforded compounds **1h** (benzene) and **1i** [benzene-$CHCl_3$ (4:1)].

Compound **1h** was crystallised from $CHCl_3-MeOH$ as needle shaped crystals, m.p. 248-49° $[\alpha]_D \pm 0°$; TNM test positive; Beilstein test negative; IR: 3500 ($-OH$), 1715, 1240 ($-O-CO-CH_3$),3040, 1640, 890 cm^{-1} ($>C=CH_2$), MS (*m/z*): 483 $[M-1]^+$, 465, 425, 424 $[M-AcOH]^+$ 408, 380, 356, 248, 233, 203, 189 (base); PMR: δ 0.78, 0.83, 0.84, 0.85, 0.94, 1.03 (6*s*, 18H, 6 × t-CH_3), 2.04 (*s*, 3H, $-OCO-CH_3$), 4.15 (q, $J_{AB}=6$ Hz, 2H, $-CH_2OH$), 4.48 (*m*, 1H, $H-C-O-C-CH_3$), 4.94 (*m*, 2H, $>C=CH_2$) (Found: C, 79.3; H, 10.8. $C_{32}H_{52}O_3$ requires C, 79.3; H, 10.81); Acetylation of **1h** with Ac_2O-Py gave the diacetate **1j**, m.p. 166-67°, $[\alpha]_D + 8°$, IR: 1750, 1730, 1250, 1265, (2 × $OCOCH_3$), 3080, 1640 and 840 cm^{-1} ($=CH_2$).

Compound **1i**: *30-hydroxy lupeol*

It was crystallised from $CHCl_3-MeOH$, m.p. 226-28°, $[\alpha]_D + 4°$; responded to TNM test but did not respond to Beilstein test. IR: 3300-3400 ($-OH$), 3100, 1640 and 880 cm^{-1} ($>C=CH_2$). (Found: C, 81.2; H, 11.4; $C_{30}H_{50}O_2$ requires C, 81.4; H, 11.4). It was identified by preparation of its diacetate **1j** ($Py-Ac_2O$), m.p. 163-64°, $[\alpha]_D + 8°$ [Lit[7] m.p. 163-64°, $[\alpha]_D + 9.7°$] which was identical with **1j** prepared from **1h**.

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