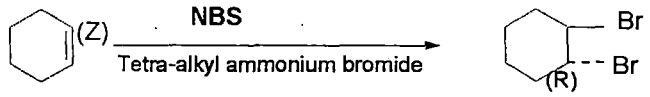
CHAPTER – I

A short review on the action of N-bromosuccinimide on triterpenoids and steroids.

A variety of rearrangements take place within the plants under different biogenetic conditions. It has been found that triterpenoids undergo these rearrangements with simple reagents also. Under various oxidative conditions some very important rearrangements take place under the influence of various reagents like N-bromosuccinimide (NBS), lead tetra acetate, organic per-acids, mercuric acetate, hydrogen peroxide etc. The present thesis includes the reaction of NBS on carbocyclic compounds. So, a brief account of previous works on oxidative transformation with NBS is given here.

Selliwano[1] prepared N-bromosuccinimide in 1893. Wohl and Jaschinowski[2] discovered the use of NBS as an allylic brominating agent in 1919. Ziegler *et al*[3] also prepared eight other bromoimide but found them to be far less satisfactory than NBS for allylic bromination. Out of many reviews on action of NBS a) Filler[4] for bromination and oxidation reactions b) Homer and Wenkelmen[5] for allylic bromination and c) Djerassi[6] for allylic bromination deserve special mention.

NBS reacts with olefins to add bromine to double bond, the addition reaction being catalyzed by tetra alkyl ammonium salts, e.g. cyclohexene reacts with NBS in presence of tetraethyl ammonium bromide to give 1,2 dibromocyclohexane as major product.



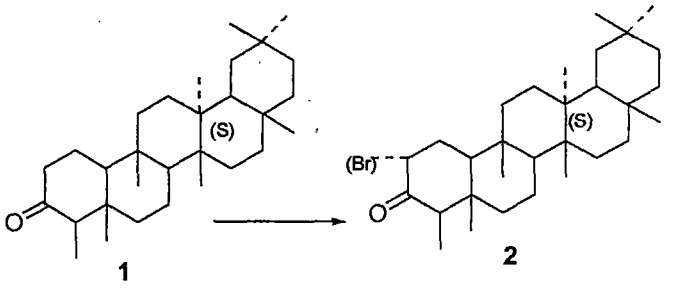
N-bromosuccinimide was used extensively since 1969 as an effective reagent for oxidation of allylic methylene to carbonyl function by Finucane,Carsano[7-9]

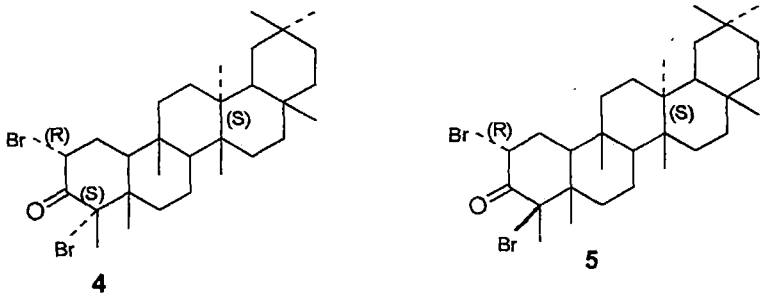
As the present thesis embodies the reaction of NBS with moretenyl acetate, diosgenin acetate, along with dimedone and benzoyl acetone it is felt necessary to give a brief review on action of NBS on some triterpenoids and steroids.

CHAPTER - I (SECTION – A)

Action of NBS on friedelin and its derivative

Corey and Ursprung[10] have reported that friedelin **1** on direct bromination gave 2α-(axial) bromofriedelin **2** and bromination of appropriate enol benzoate gave the isomeric 4α -(axial) – bromofriedelin **3**. A dibromo friedelin **4** was also prepared by them by reaction with HBr in $CHCl_3$ and was assigned as 2α, 4α - dibromo friedelin from UV spectra at 332nm. Bromination of 2α - bromofriedelin in acetic acid was carried out by Djerassi *et al*[12] which furnished another dibromo friedelin **5**. From the studies of UV (310.5nm.) and ORD, it was designated as the 2α, 4β - dibromo friedelin.

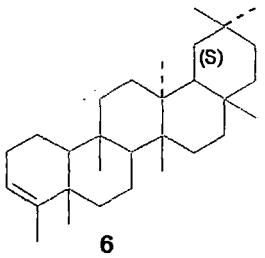




Takahasi and Qurrison[13] also prepared a dibromo friedelin by the action of bromine in chloroform and acetic acid on friedelin. However, they could not assign the structure of this compound although the compound showed UV absorption at 320 nm.

Stevenson *et al*[14,15] reported that friedelin **1** on treatment with molar equivalent of NBS in carbon tetrachloride gave 4α-bromofriedelin **3**. They also isolated 2α - bromofriedelin **2** from 3 by further treatment of **3** with bromine in acetic acid. Hence in this reaction isomerisation occurred. However, as expected 4α-bromofriedelin **3** was unstable in chloroform-hydrobromic acid.

Since this route was not successful for obtaining dibromo friedelin, an alternative method of treatment of 2α - dibromo friedelin with NBS was carried out. Treatment of 2α- bromofriedelin with NBS gave an unsaturated monoketone $C_{30}H_{47}OBr$ that showed positive T.N.M. test suggesting thereby the presence of ethylenic linkage. The fact that double bond was not conjugated to carbonyl group and the α-bromine atom retained an axial orientation was proved by UV and IR spectra of the ketone. Since it was known that acid-isomerisation of friedel 3-ene **6** afforded a mixture of olean-13 (18)-ene,**7** and 18α-olean-12 –ene, **8,** it was assumed that this non-conjugated bromo ketone had probably arisen by molecular rearrangement of 2α,4α-dibromo ketone intermediate with elimination of hydrobromic acid.



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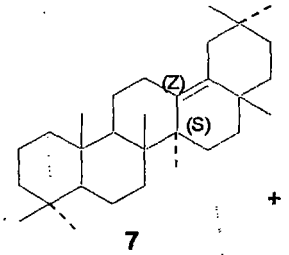

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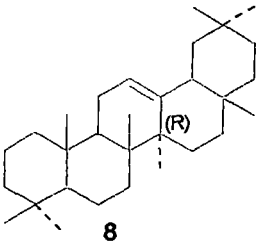

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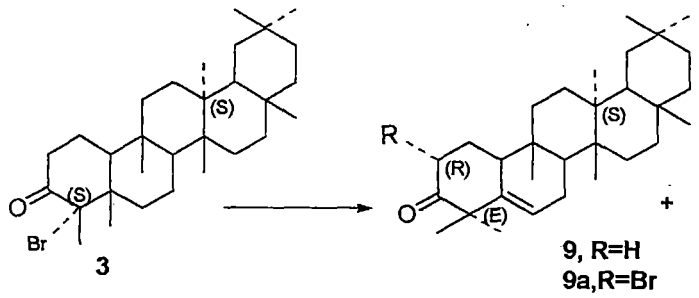
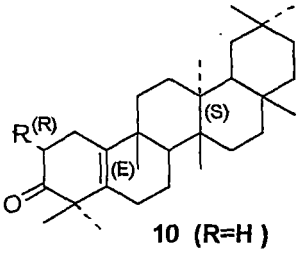
A precedent for such a rearrangement was provided by the action of silver acetate on 4α-bromofriedelin **3** to give a product **7** which was shown to be a mixture of alnus-5-enone,**9** (R=H) and alnus –5(10)-enone **10** (R=H)



3

9, R=H
9a,R=Br



10 (R=H)

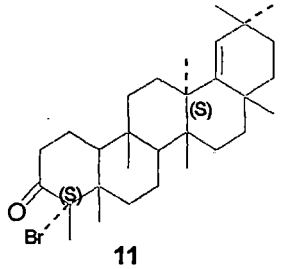
The probability that unsaturated bromo ketone derived from **2** could be represented as 2-bromo alnus-5enone **9a** was excluded from the fact that the zinc debromination product in neutral solution was different from either **9** or **10**.

Treatment of 4α-bromofriedelin **3** with NBS gave an isomeric non-conjugated axial bromo substituted ketone **11** $C_{30}H_{47}OBr$ that on dehydrobromination gave a compound identical with $C_{30}H_{48}O$ **12**. **12** on lithium aluminum hydride reduction gave an alcohol **16** and on Huang Minlon reduction gave the hydrocarbon **15**. From these observation isomeric monobromoketones obtained from **2** and **3** were assigned 2α bromofriedel-18 en-3-one **13** and 4α bromofriedel-18-en-3-one **11** respectively. The assignments were supported by specific rotation and ORD studies.

R.Stevenson et al[11,17] reacted Friedelane **14** with NBS and an unsaturated hydrocarbon **15** was found that was identical in all respect with that obtained from Huang Minlon reduction of **12.** This fact suggested that the products obtained by the action of NBS on ketone **2** and **3** were ethylenic non-conjugated ketones and hence the attack has taken place at a site not activated by carbonyl group, **15** yielded an oxide $C_{30}H_{50}O$ with per benzoic acid but resisted catalytic hydrogenation, which showed that double bond has a degree of steric hindrance comparable to the Δ12 /trisubstituted ethylenic linkage in β-amyrin series. Terminal UV absorption of **12,15** and **16** indicated that the double bond was trisubstituted. The fact that **15** resisted catalytic hydrogenation suggested that ethylenic system was not disubstituted and friedelin skeleton does not permit the existence of a tetra-substituted double bond.

^{1}H NMR spectrum of ketone **12** showed a singlet that attributed to an olefinic proton not conjugated with carbonyl group. The location of double bond on bromo ketones **2,3** and hydrocarbon **15** was thus restricted to position 1(10),7 or 18. The position 1(10) and 7 were discarded by dehydrobromination of **11** with silver acetate. A dehydrobrominated product $C_{30}H_{45}O$ was isolated which gave UV absorption above 220 nm. Since there was no conjugation of carbonyl or ethylenic functions in this dienone, the original double bond could not be located in ring A and B. There had been much work on the synthetic application of allylic compounds.

Comparatively little was known about the action of NBS on saturated systems. It has been proved that cyclohexane and cycloheptane yield cycloalkyl bromide with NBS under certain condition and decalin gave a tetrabromo octa hydronapthalene which can also be obtained from probable intermediate 9, 10 octalin.



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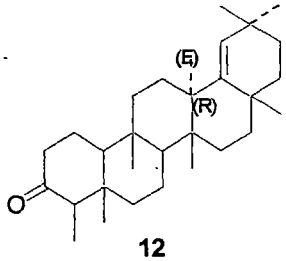

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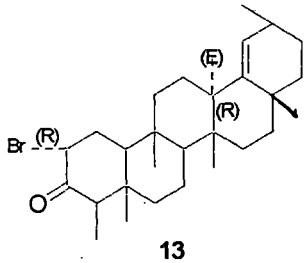

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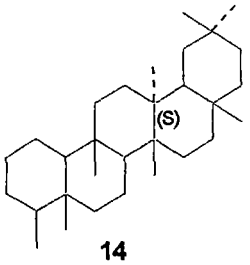

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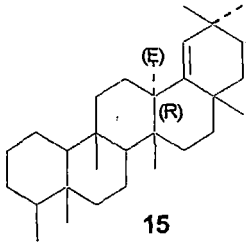

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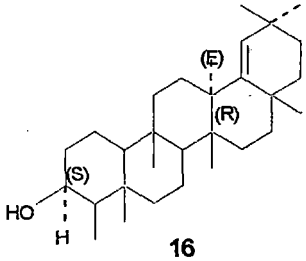

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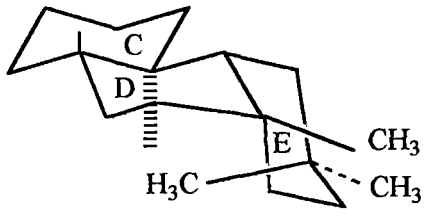
Cason *et al* [23] established that in friedelin the tertiary α-hydrogen atom at position C-4 was more reactive than secondary hydrogen atom at position 2 but the presence of a 2α-bromine atom effectively prevented the abstraction of a 4α-hydrogen atom by its 1,3-diaxial blocking effect to approaching succinimide radical. In absence of the activating C-3 carbonyl group or if there is a deactivation due to the steric influence of the neighboring axial halogen , the most reactive hydrogen is the tertiary C-18. An examination of all chair form **17** of friedelane showed that a severe steric interaction must exist between the 13α and 20α-methyl groups due to its *cis*-junction at rings D and E. This interference is removed if the terminal E ring adopted a boat configuration **18**, but as a consequence and unfavorable 1,4- diaxial boat prow and stern interaction results. The steric strain inherent in both conformations with *cis* D/E system is relieved by dissociation of the 18β -hydrogen atoms and formation of ethylenic trigonal system.



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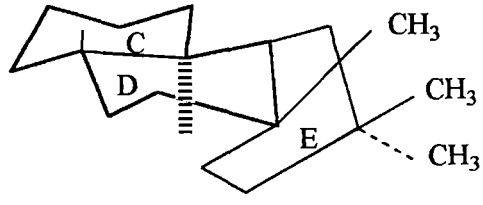

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CHAPTER I (SECTION-B)

Bromine and NBS oxidation of saturated hydrocarbon, friedelane [18].

NBS is the most common of all other reagents for halogenation of olefins in allylic position. An initiator, usually peroxide is needed with this reagent. The reaction is quite specific at allylic position with usually a good yield, in unsymmetrical allylic radical intermediate however allylic shifts can take place and a mixture of both possible products are obtained.

$$H_3C\text{-}CH_2\text{-}CH=CH_2 + NBS \rightarrow H_3C\text{-}\underset{\displaystyle Br}{CH}\text{-}CH=CH_2 + H_3C\text{-}CH\text{-}CH\text{-}CH_2\text{-}Br$$

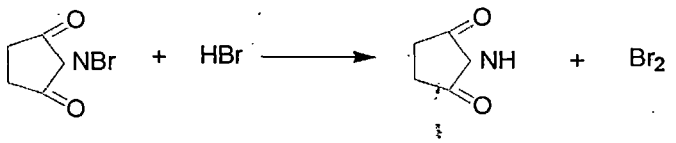
In case a double bond has two different α positions (e.g. $H_3C\text{-}CH=CH\text{-}CH_2\text{-}CH_3$) a secondary position is substituted more readily than the primary.

Douben and McCoy[19] demonstrated that the mechanism of allylic bromination is of the free radical type. They showed that the reaction was very sensitive to free radical initiators and inhibitors and the reaction stopped unless at least a trace of initiators was present. Further work indicated that the species that actually abstract hydrogen from the substrate is the bromine atom. The reaction is initiated by small amount of bromine, once it is formed, the main propagation steps are:

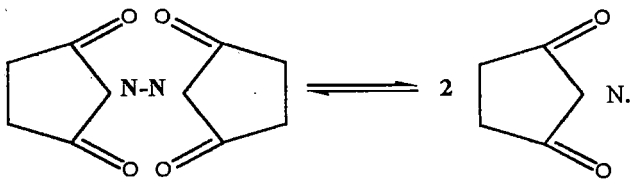
$$1.\ Br^0 + RH \rightarrow R^0 + HBr$$

$$2.\ R^0 + Br_2 \rightarrow RBr + Br^0$$

The source for bromine is a fast ionic reaction between NBS and the HBr liberated in step 1.

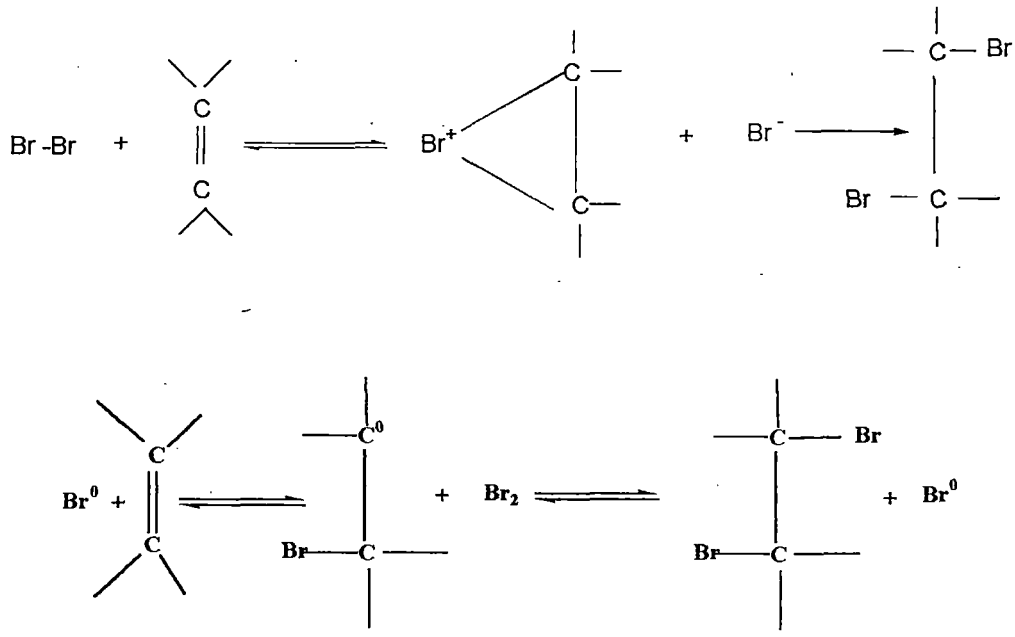


The formation of NBS is therefore to provide a source of Br_2 in a low steady state concentration and then use up the HBr liberated in step 1. Previously it was supposed that the abstracting species was the succinimide radical **18a** but there is no much evidence that this species is involved in the reaction. The main evidence is that NBS and bromine show similar selectivity that the various N-bromosuccinimide also show similar selectivity which would not be the case if a different species was abstracting in each case and that **18a** has proved itself to be a much less stable species than that was originally thought, since its dimmer show no tendency to dissociate.



18a

The reacting species Br_2 does not add to the double bond either by an ionic or free radical mechanism. The concentration of bromine being too low in the addition of double bond only one attacking bromine atom of a bromine molecule is being attached to the substrate, whether the addition is electrophillic or free radical.



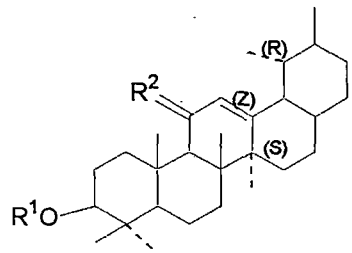
Another bromine molecule supplies the other bromine. There will not be a high probability that the proper species will be in the vicinity once the intermediate forms and the equilibrium will lie to the left in case the concentration of bromine is sufficiently low. So, the rate of addition is slow and the allylic substitution goes to completion successfully, if this is true then it should be possible to brominate an olefin in the position. McGrath et al[30] demonstrated that even in case of NBS or similar compound if a very low concentration of bromine is used and if the HBr is removed as it is formed, so that it is not available to complete the addition step, bromination in allylic position is possible.

Stevenson *et al*[11,17] obtained friedel -18-ene **15** by the oxidation of friedelane **14** by NBS. They compared action of bromine on **14** in carbon tetrachloride solution in order to explain the fact that the function of NBS was to provide molecular bromine. A solution of bromine in carbon tetrachloride was added to friedelane, the colour of bromine being discharged and the reaction mixture was worked up in usual way. Friedel-18-ene **15** was obtained in a comparative yield, which indicated that succinimide radical was not essential. Chromatographic examination revealed that there was no unchanged friedelane. However, an unstable bromofriedelane was isolated that changed readily into friedel-18-ene. The compound was considered to be 18-bromofriedelane. The discrepancies and poor reproducibility reported [11a] in the bromination of 3-ketone friedelin by NBS particularly in the formation of di and tribromo derivatives at C-2 and/or C-4 may be attributed to accompanying halogenation at C-18.

CHAPTER I (SECTION – C)

Oxidation of allylic methylene to carbonyl group by NBS

Corsano *et al*[31] reported the formation of 3β - acetoxy-urs 12 -en-11-one **20** in 80% yield by direct oxidation of α-amyrin acetate **19** with NBS in aqueous dioxan solution.

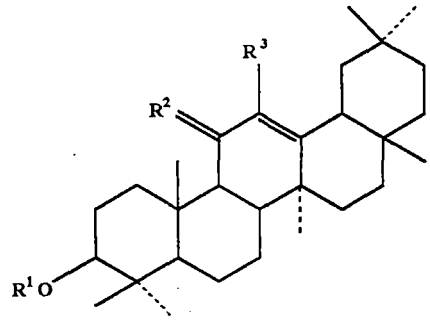


19 R^1 = Ac, R^2 = H

20 R^1 = Ac, R^2 = O

Finucane and Thompson [32,33] showed that the allylic methylene could be converted to carbonyl group by direct oxidation of former by NBS in the presence of visible light. According to them trisubstituted olefins containing an allylic methylene group when treated with NBS in aqueous dioxane followed by irradiation with visible light, α,β-Unsaturated ketones were obtained in near quantitative yield. Finucane *et al* [32] treated β-amyrin acetate **21** with NBS in aqueous dioxane in a typical ambient light experiment as described by Corsano *et al* [31]. On chromatography over silica gel they isolated starting material (ca 40%), bromo compound (ca 8%) and 3β-acetoxy olean 12–ene-11α-ol **23** (ca 2%). Oxidation of **23** with CrO_3 in acetone afforded 3β-acetoxy olean–12-en–11–one **22**.

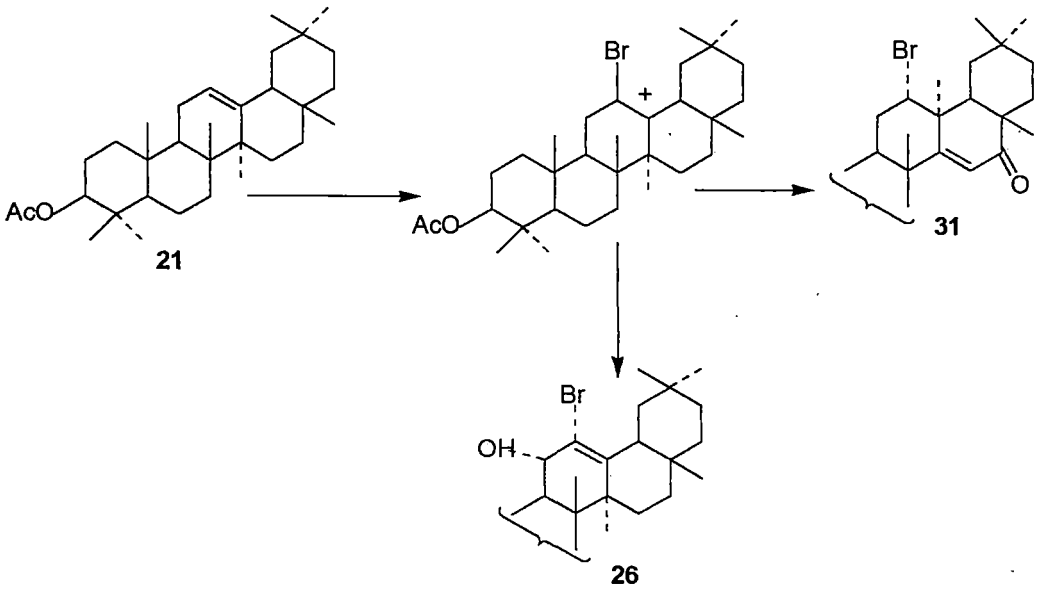
In another experiment the products were isolated by chromatography over alumina.The compounds thus isolated were amyrin acetate 21 (ca 35%), 3β-acetoxy–olean–12–en-11-one **22** (ca 40%), bromo compounds (ca 10%) and polar materials (ca 10%). The polar fraction was eluted with methanol, acetylated and rechromatographed. The products thus isolated were 11α-methoxy–Olean–12–en-3β-yl acetate **24**,11β-hydroxy–olean–12–en-3β-yl acetate **23**and olean – 9 (11),12-dien-3β-yl acetate **27** and a trace of 3β-11α-diacetate **25**. The α-methoxy acetate **24** with p-toluene sulphonic acid in acetic anhydride yielded 3β-acetoxy-olean-11 (12), 13(18)-diene **29** in quantitative yield.



21 R^1 = Ac, R^2 = H_2, R^3 = H
22 R^1 = Ac, R^2 = O, R^3 = H
23 R^1 = Ac, R^2 =OH, R^3 = H
24 R^1 = Ac, R^2 =a-OMe, R^3 = H
25 R^1 = Ac, R^2 =a-OAc, R^3 = H
26 R^1 = Ac, R^2 =a-OH, R^3 = Br
27 R^1 = Ac, R^2 = O, R^3 = Br
28 R^1 = Ac, R^2 =H_2, R^3 = Br
29 R = H
30 R = Br

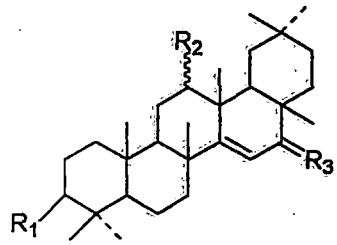
The bromo compounds were resolved by chromatography over alumina and fractionally crystallized into two components. The major product was a diol mono acetate ($C_{32}H_{51}O_3Br$) which was identified as 3β-acetoxy-12-bromo-olean-12-en-11α-ol **26** from UV, NMR, TNM test and further acetylation. The minor component of the mixture of bromo compounds was identified as 12α-bromo-16-one **31**- from UV (λmax, 244nm) and NMR spectra. The mechanism proposed for the formation of **26** and **31** suggested that the initial α -face attack on β-amyrin acetate **21** at C-12 would lead to carbonium ion.

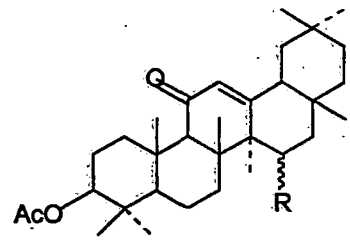
Elimination of a proton from C-12 followed by allylic hydroxylation would then lead to **26**. Alternatively migration of 14α -methyl group to C-13, elimination of a proton from C-15 and subsequent allylic oxidation would give the 12α-bromo 16-one **31**.



Thomson *et al* [33], subjected taraxeryl acetate **32** to oxidation following the method adopted by Corsano *et al* [31], and obtained two different products. The major product was assigned the structure of 16-oxo-taraxeryl acetate **33** and 16β-hydroxy-taraxeryl acteate **34.** An unsaturated ketone **33** was obtained by reaction of **34** with chromic acid in acetone.

Oxidation of taraxeryl acetate in aqueous dioxane for five and half hours in presence of $CaCO_3$ in visible light give compound **36**,11-keto-15-bromo-β-amyrin acetate, which in turn gave a halogen free compound **37** with Zn dust and acetic acid. Its structure was established as β-amyrenonyl acetate **37**.





32 R_1=OAc, R_2=H, R_3=H_2 **36** R=Br

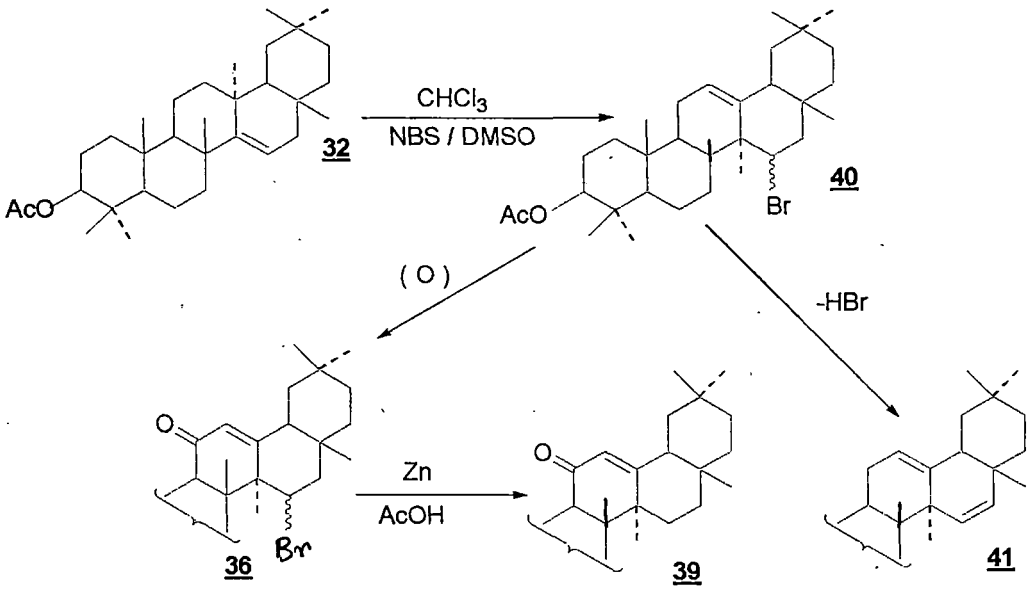
33 R_1=OAc, R_2=H, R_3=O **37** R=H

34 R_1=OAc, R_2=H, R_3=β-OH,α-H

35 R_1=OAc, R_2=Br, R_3=O

Khastagir *et al* [34] repeated the oxidation of taraxeryl acetate **32** with NBS in aqueous dioxane following method of Finucane and Thompson [33] but product isolated were different. The mixtures of two products were separated by chromatography over silica gel. The first solid $C_{32}H_{49}O_3Br$ m.p.238-40^0 was characterized as 15-bromo-amyrenonyl acetate **38**. Khasstagir *et al* following the method of Dalton and Jones [35] found that taraxeryl acetate **32** on treatment with aqueous dimethyl sulphoxide in chloroform and NBS in dark afforded a solid $C_{32}H_{51}O_2Br$, m.p. 180-82^0 with no UV absorption between 220-300 nm.

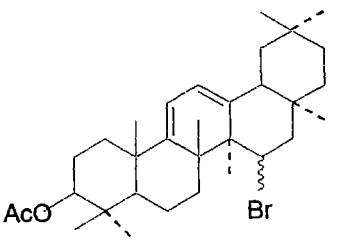
The structure of 15-bromo compounds was assigned to be **40** from IR, NMR and mass spectra. The bromine atom at 15 positions of **40** would be expected to have the same stereochemistry as in the case of product from NBS-aqueous dioxane oxidation method. Compound **40** on oxidation with CrO_3- AcOH gave **38** m.p. 238-40^0 identical with the product obtained from NBS- aqueous dioxane method.



Dehydrobromination of **40** with KOAc in acetic acid at 130^0 for four hours gave the product $C_{32}H_{50}O_2$, m.p. 199-200^0 C. The same compound was obtained when **40** was refluxed with dimethylaniline for six hours. The structure **41** was proposed to it.

The second compound $C_{32}H_{50}O_3$ m.p. 280-82^0 C was devoid of bromine and showed UV (λmax 245 nm), IR (peaks at 1730,1680,1250 cm.$^{-1}$), Mass peak (M^+ 482) and NMR spectrum (peaks at δ5.85, 2.10, 4.5 ppm.). So the compound was designated as 16-oxo-taraxeryl acetate **33**, although its m.p. was different from that recorded by Finucane and Thomson[33].

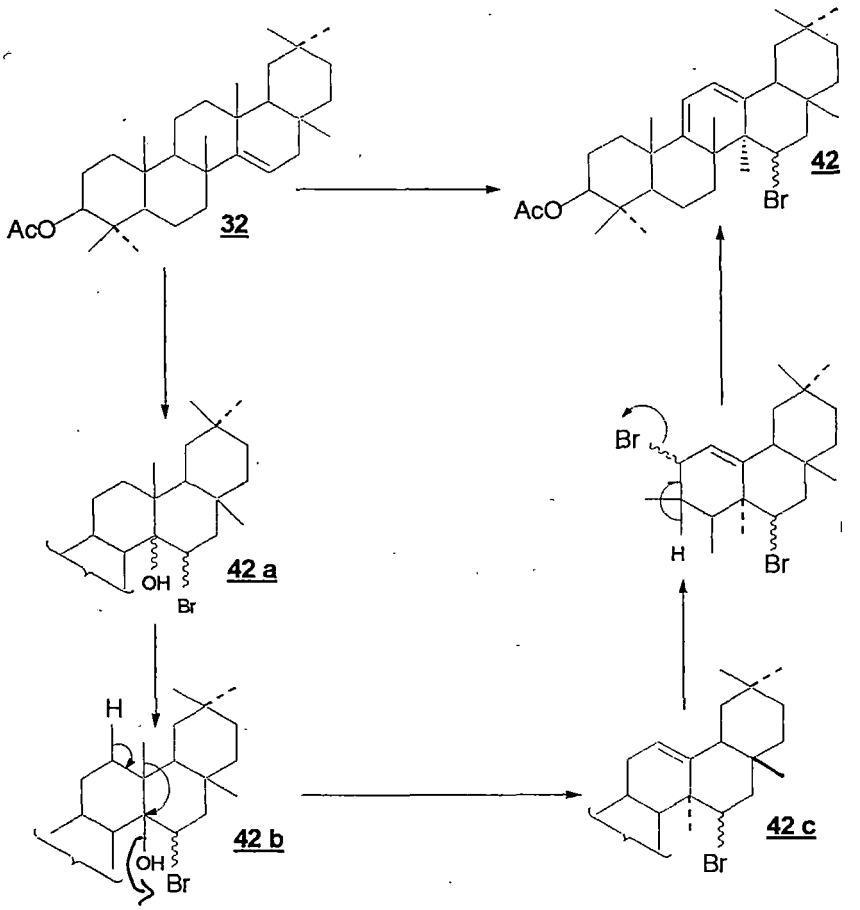
The third product $C_{32}H_{49}O_2Br$, m.p. 176-178^0 C showed UV (λmax 276 nm), NMR (δ5.34 & 5.85 ppm.) and a sharp signal at 2.08 ppm. (-O.Co.CH_3) and multiplet at δ 4.6 ppm. (-CH.O.$COCH_3$) and the compound was assigned structure **42**.



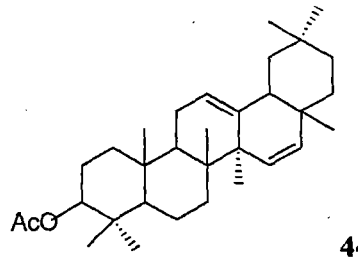
42

The mechanism for formation of **42** from **32** was suggested as in **Scheme- I**:

Scheme-I



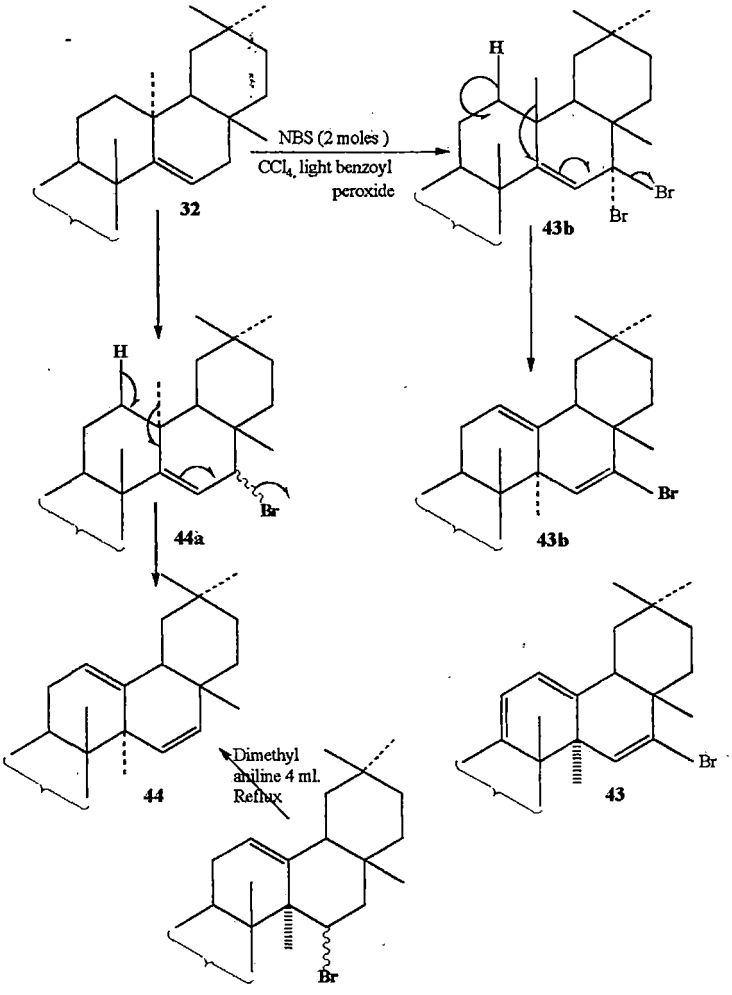
Khastgir *et al.* [34] studied the reaction of taraxeryl acetate **32** with 2 moles equivalent of NBS in CCl_4 and benzoyl peroxide in presence of visible light for three hours and isolated a product having structure **44** identical with compound obtained by dehydrobromination of **40.**



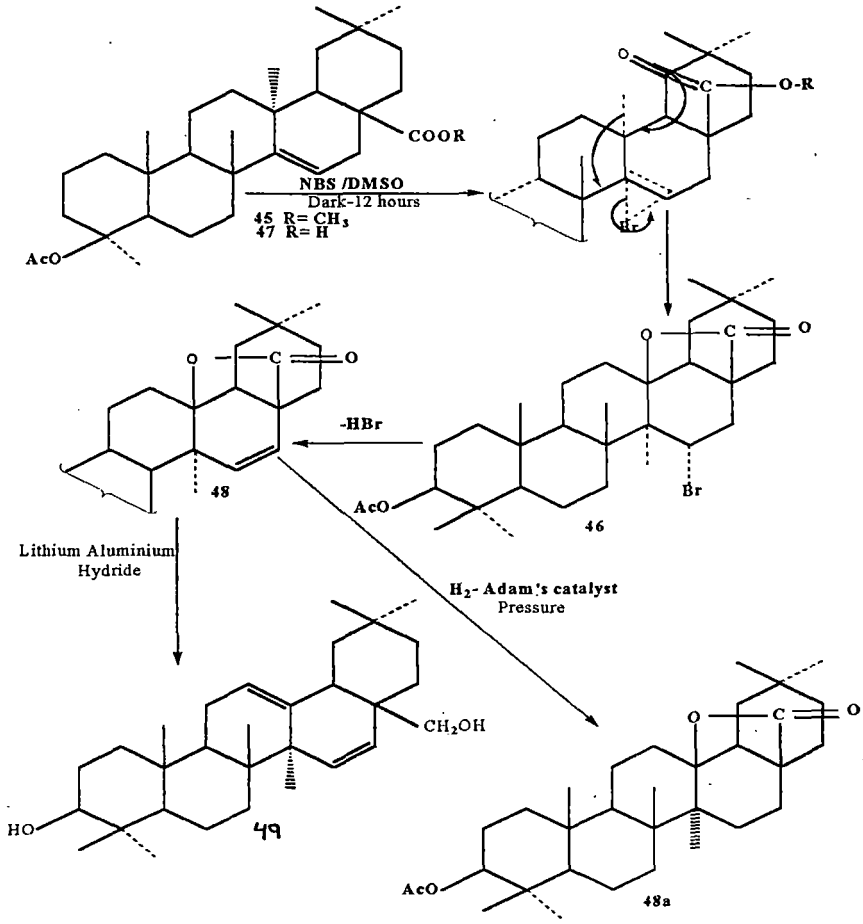
44

Scheme-II below represents the proposed mechanism for formation of **43** and **44**.

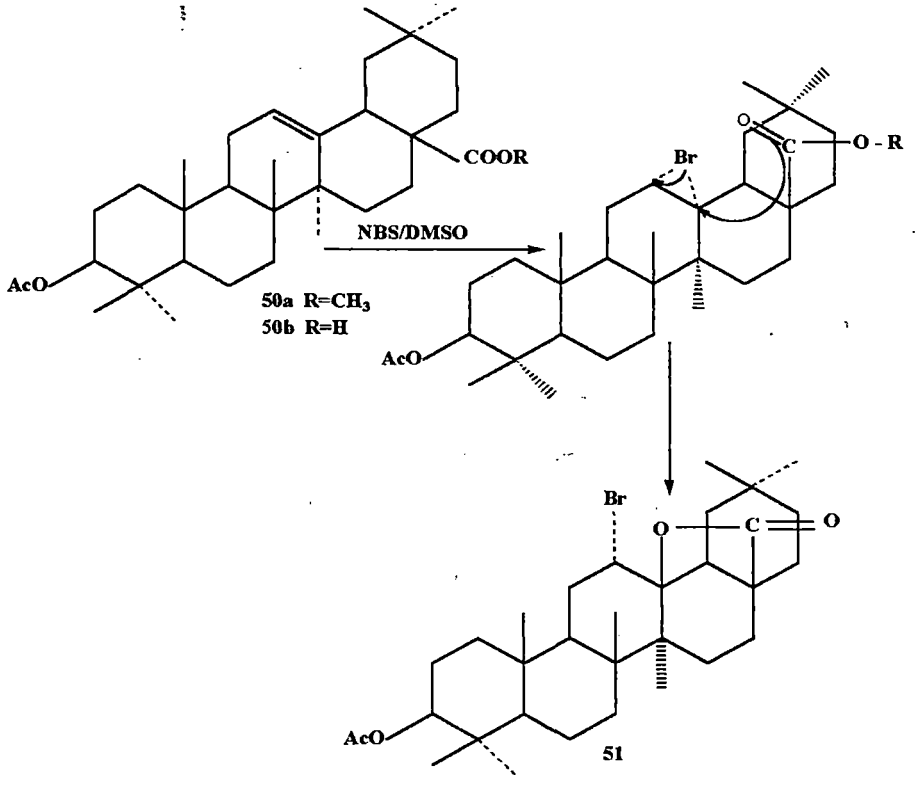
Scheme- II



Pradhan *et al* [37] studied the reaction of acetyl methyl aleuritolate **45** with NBS in dimethyl sulphoxide in dark for 12 hours and isolated a bromo lactone **46**. On dehydrobromination with dimethylaniline **46** afforded 15-dehydrolactone **48** which on LAH reduction furnished aegiceradiol **49**, $C_{30}H_{48}O_2$ m.p. 235^{0}C. Catalytic hydrogenation of **48** with Adam's catalyst in acetic acid under pressure afforded 3β-acetyl oleanan-28, 13-olide **48a**. Pradhan et al also isolated same bromolactone **46** by repeating reaction on acetyl aleuritolic acid **47**. According to them formation of **46** probably involved attack of bromonium ion from NBS in DMSO at the double bond. Bromine assumed equatorial position to avoid maximum strain and steric interaction. Migration of C-13 methyl to C-14 position and elimination of methoxy methyl occurred to give **46**.

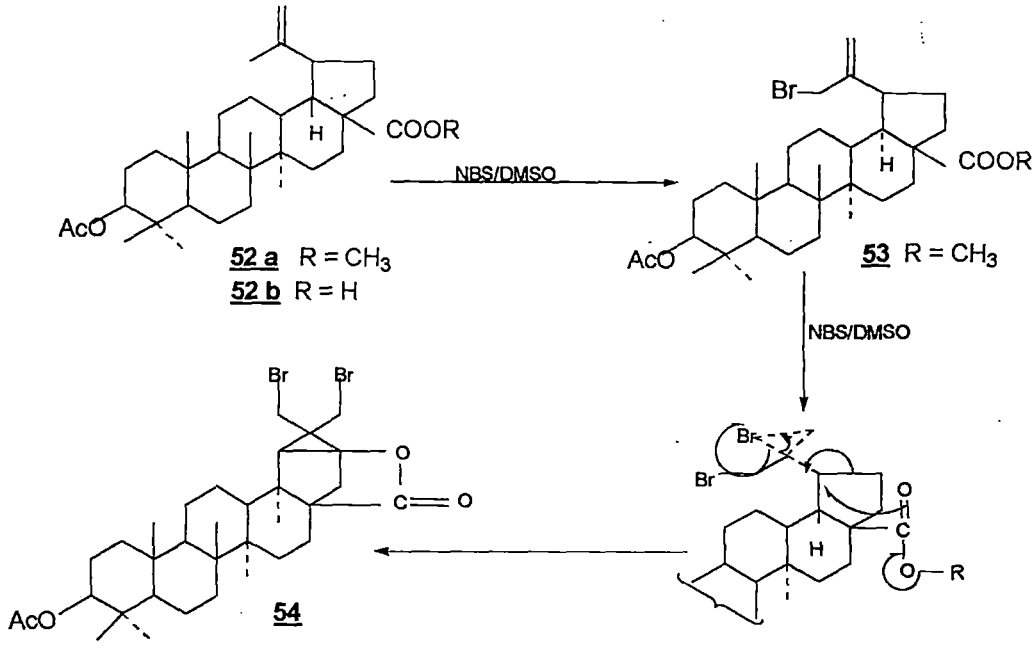


Acetyl methyl oleanolate **50a** and 3β-acetyl oleanolic acid **50b** under the same condition with NBS in DMSO gave the same bromolactone **51** which was found to be identical with 3β -acetyl-12α -bromo-oleanan-28-13 – olide .

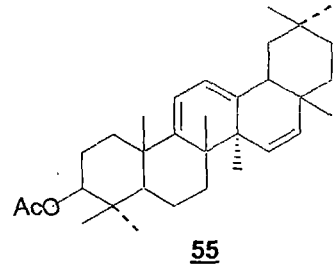


Pradhan *et al* found two different bromo compounds when 3β-acetyl methyl betulinate **52 a** was reacted with NBS in DMSO under similar conditions. The more polar fraction was identified as dibromolactone **54** with molecular formula $C_{32}H_{48}O_4Br_2$, m.p.303 – 304 °C. The structure assigned was 3β- acetyl-29, 30 dibromo-18 α-H,oleanan 28 19 β-olide. The less polar fraction $C_{33}H_{51}O_4Br$, m.p. 235-236 °C was identified as methyl-30-bromo-3β-acetyl betulinate **53** .The following **Scheme III** represents the proposed mechanism for formation of **54**.

Scheme III

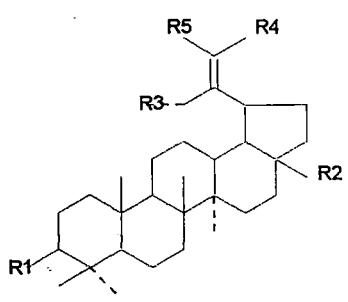


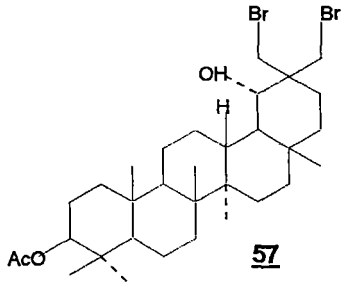
Anjancyulu *et al*[40] adopting method of Finucane and Thompson[32] subjected taraxeryl acetate **32** to NBS in aqueous dioxane. Two products out of four were identified as **43** and **48** by physical means. The third compound was assigned the structure 3β-acetoxy–oleanan – 9,12,15- triene and fourth compound was identified as 3β-ol of **55**.



55

Pradhan *et al*[41] also reported the action of NBS on lupenyl acetate **56** in DMSO and isolated four different compounds which were 30-bromo lupenyl acetates **56 a**, 29 (E-Z) –bromo lupenyl acetates **56b** and **56 c** and 29,30 dibromo-18-iso-oleanan-19α hydroxyl-3β- yl-acetate **57**.





57

56 $R^1 = OAc, R^2 = CH_3, R^3 = R^4 = R^5 = H$

56a $R^1 = OAc, R^2 = CH_3, R^3 = Br, R^4 = R^5 = H$

56b $R^1 = OAc, R^2 = CH_3, R^4 = Br, R^3 = R^5 = H$

56c $R^1 = OAc, R^2 = CH_3, R^5 = Br, R^3 = R^5 = H$

56d $R^1 = OH, R^2 = CH_3, R^3 = O, R^4 = R^5 = H$

56e $R^1 = OH, R^2 = CH_3, R^5 = Br, R^3 = R^4 = H$

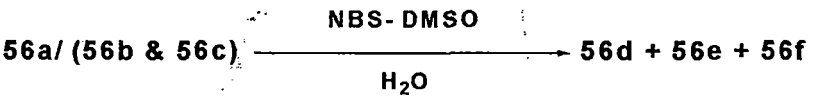
56f $R^1 = OH, R^2 = CH_3, R^4 = Br\ R^5 = R^3 = H$

56g $R^1 = OAc, R^2 = CH_3, R^3 = OH, R^4 = R^5 = H$

56h $R^1 = R^3 = OH, R^2 = CH, \quad R^4 = R^5 = H$

Compound **56a** on alumina afforded 30- hydroxy lupenyl acetate **56g** and 30 hydroxy lupeol **56h**.

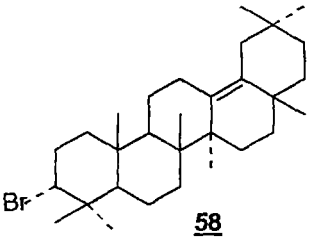
Compound **56a** and mixture of **56b** and **56c** with NBS in DMSO containing water afforded 30-oxo-lupeol **56d** and 20 (E-Z)-bromo lupeol **56e** and **56f** respectively.



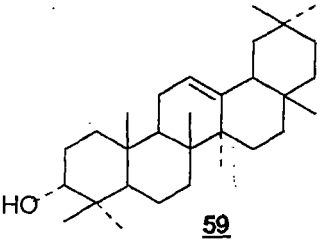
Appearance of doublet at δ 4.01 ppm in ^{1}H NMR spectrum was the most confusing feature of the compound **57** because it was expected to give a singlet if the hydroxyl group is situated at C-19 position. So the most likely position of the location of this hydroxyl group could be C-21 which would then explain the appearance of this doublet at δ 4.01 ppm.In order to make an unambiguous decision of the structure of the compound **57** two derivatives viz. keto and acetate have been prepared. The structure of dibromohydroxy compound **57** was confirmed from the ^{1}H NMR of keto and acetate.

The formation of dibromo hydroxy compound **57** has been proposed to take place by the following rearrangements of lupine system to oleanan system. The mechanism proposed has been represented in **Scheme IV**.

Pradhan *et al*[42] further reported the action of N-bromosuccinamide on friedel -3 (4)- ene in dimethyl sulfoxide and isolated two compounds **58** & **59** . **58** was assigned the structure 3α- bromo olean -13(18)-ene and **59** was assigned the structure 3β-hydroxy olean-12 (13)- ene.

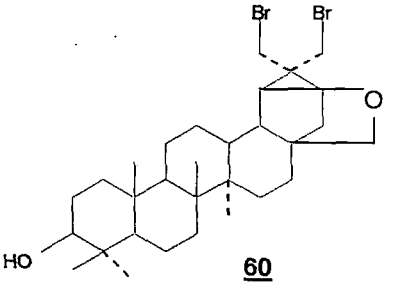


58



59

Pradhan *et al* [43] reported the action of NBS on lupan–20 (29) – ene 3β, 28–diol in dimethyl sulfoxide and isolated the compound **60** which was assigned the structure 3β–hydroxyl olean–28–19–oxo-29,30–dibromide.



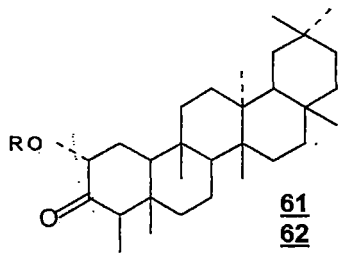
60

Pradhan *et al* [44] have further extended their investigation on the action of NBS and DMSO on Cerin **61** and Cerin acetate **62**. Cerin **61** furnished two compounds. The first compound was identified as 1,1-dibromo-2 keto friedel–3(4)–en-3 ol **61a** m.p. 234 -235^0 C, IR – 3385 cm^{-1} and 1655^{-1} (for hydroxyl group and α, β – unsaturated carbonyl group) UV– 273 nm , PMR δ 1.84 (s) (for methyl on olefinic double bond), δ 3.24 (s) (for C-10 proton), δ6.62 (s) (for OH on olefinic double bond). Acetylation of the compound gave an acetate m.p. 242 – 243^0 C, IR 1750 cm^{-1} and 1680 cm^{-1} (for acetate carbonyl and α ,β unsaturated ketone respectively) , PMR : a singlet at δ 1.81 (for methyl protons on the olefinic double bond) , a singlet at δ 2.4 (for acetoxy protons) a singlet at δ 3.4 (for C_{10}- H).

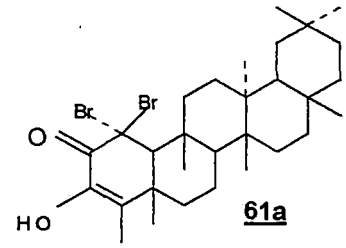
Another compound was identified by spectral analysis as friedel–1, 3–dien-2,3-diol **61b** m.p. 172 – 173^0 C, IR – 3380- 3460 cm^{-1}for hydroxyl group, UV 292 nm. The enolic hydroxyl group was confirmed by $FeCl_3$ test, PMR – δ 1.85 (for olefinic methyl protons), two doublets at δ 6.1 and 2.69 (for C-1H and C-10H respectively).

Cerin acetate **62** on similar treatment furnished compounds 23-bromo–2 acetoxy friedel–1(2), 4(23)–dien–3one **62a** and 2α--acetoxy friedel–3(4)–en-3–hypobromite **62b**. **62a** had m.p. 177 – 178^0 C and responded +ve to Beilstein test . UV spectrum 292 nm IR – 1738 and 1235 cm^{-1} (for presence of acetate carbonyl) and 1700 cm^{-1} (α ,β unsaturated carbonyl group) PMR – a singlet at δ 2.3 (for acetoxy protons on an olefinic double bond), a singlet at δ 5.38 (for an olefinic proton without having any neighbouring proton), and doublets at δ 6.1 and 2.69 (for protons attached to C-1 olefinic carbon C-10 tertiary carbon respectively)

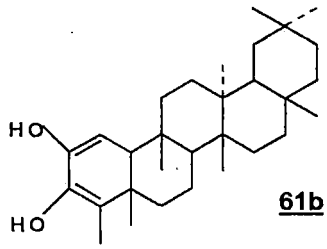
62b gave positive Beilstein and $FeCl_3$ test that indicated presence of bromine and enol system in the compound UV 220-300 nm IR 1740 and 1230 cm^{-1} (for acetoxy carbonyl) and 710 cm^{-1} (for tetra substituted double bond) PMR δ 1.01 contain six protons showing the presence of eight tertiary methyls, a singlet at δ 2.13 (for acetoxy methyl protons)



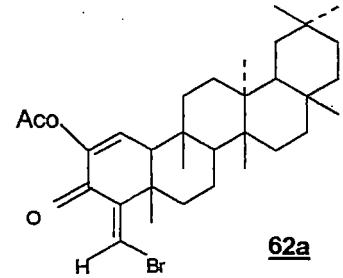
61 R = H
62 R = Ac



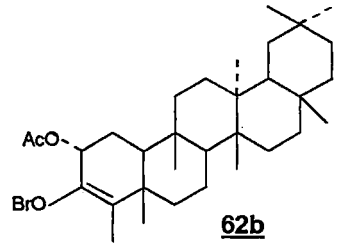
61a



61b



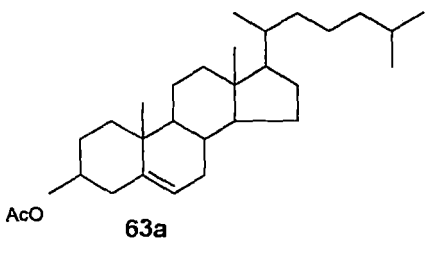
62a



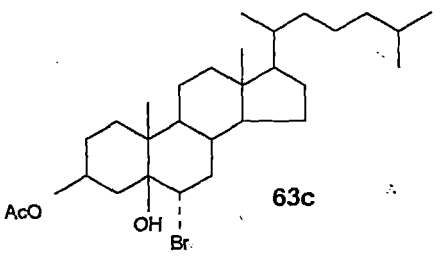
62b

Action of N- bromosuccinimide on cholesteryl acetate

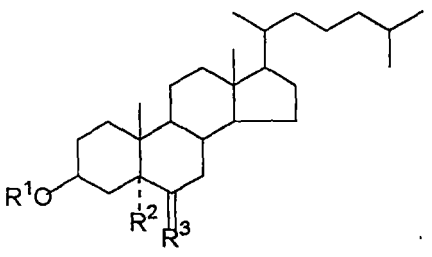
Pradhan *et al*[45] showed that cholesteryl acetate **63a** on oxidation with NBS in DMSO furnished six different compounds which were identified as 5α–bromo–6-keto cholestan- 3β-yl acetate **63b**, 6α bromo-5β hydroxy coprostan-3β-yl acetate **63c** , 5α hydroxy-6-keto- cholestan-3β-yl acetate **63d**, 5α, 6β–dihydroxy cholestan-3β-yl acetate **63e** ,3β,5α dihydroxy cholestan-6-one **63f** and cholestane-3β,5α, 6β triol **63g** by chemical studies and spectral data (IR , mass , PMR and ^{13}C NMR).



63a



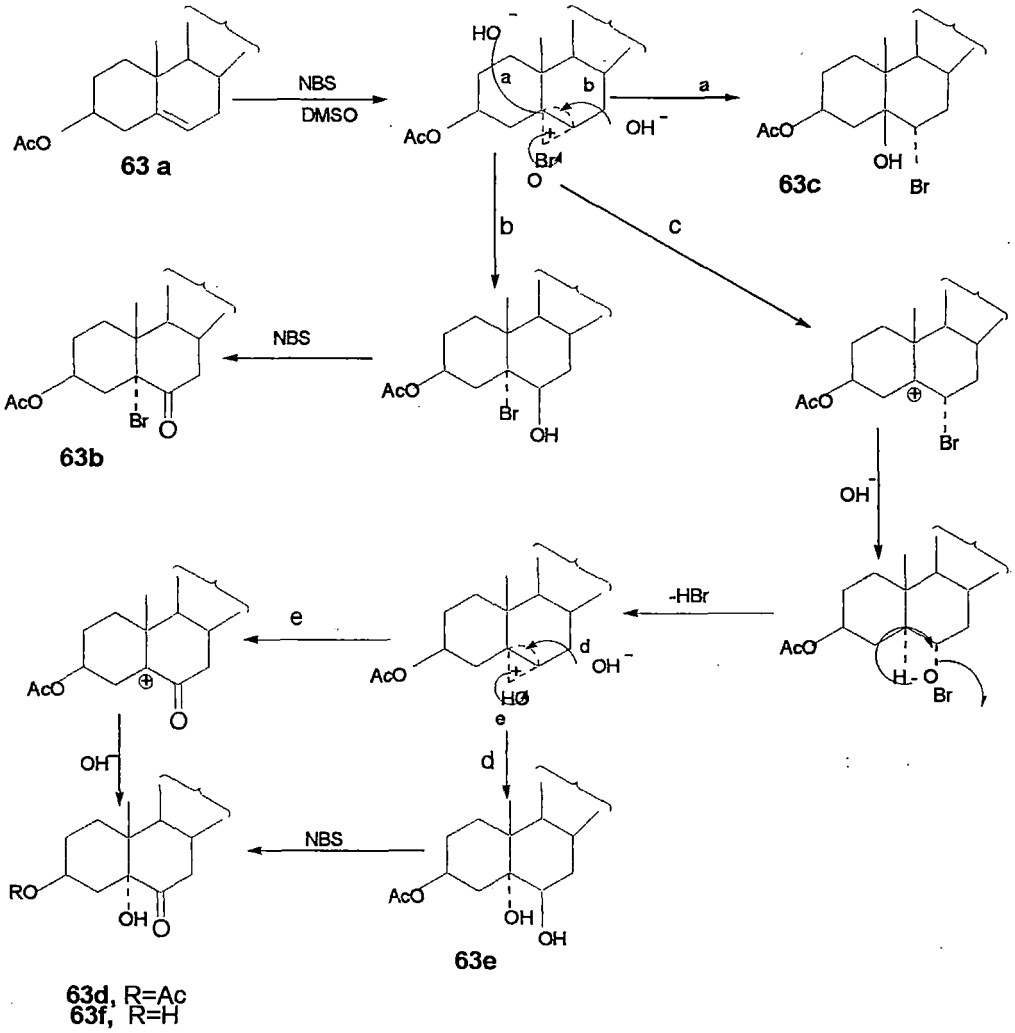
63c



63b	R^1 = Ac,	R^2 = Br,	R^3 = O
63d	R^1 = Ac,	R^2 = OH,	R^3 = O
63e	R^1 = Ac,	R^2 = OH,	R^3 = H, OH
63f	R^1 = H,	R^2 = OH,	R^3 = O
63g	R^1 = H,	R^2 = OH,	R^3 = O, H, OH

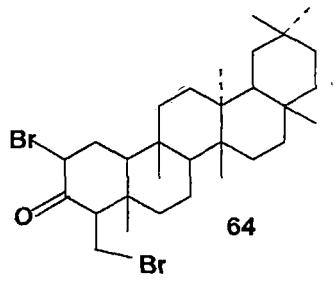
The mechanism proposed for their formation can be represented by the **Scheme-IV** below :-

SCHEME-IV



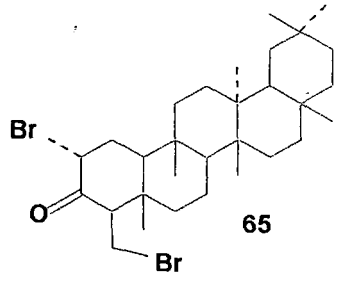
Pradhan *et al*[46] studied the action of NBS on friedelin in DMSO and found six different compounds.

Compound **64** eluted by petrol responded to Beilstein test and was analyzed for $C_{30}H_{48}OBr_2$ and was identified as 2β, 23 dibromofriedelin.



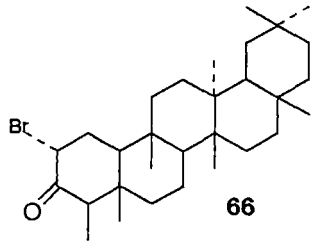
64

Compound **65** eluted by pet-benzene (9:1) was analyzed for $C_{30}H_{48}OBr_2$ and was identified as 2α, 23 –dibromofriedelin.



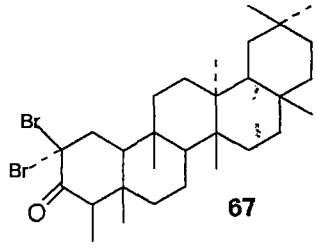
65

Compound **66** eluted by pet-benzene (9:1) was analyzed for $C_{30}H_{49}OBr$ and was identified as 2α bromofriedelin



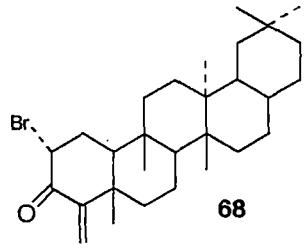
66

Compound **67** eluted by pet-benzene (9:1) was analyzed for $C_{30}H_{48}OBr_2$ and assigned structure 2α, 2β dibromofriedelin.



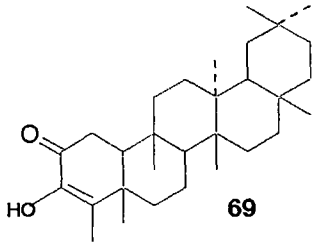
67

Compound **68** eluted by pet-benzene (3:2) was analyzed for $C_{30}H_{47}OBr$ and identified as 2α–bromo 4 (23)–dehydrofriedelin.



68

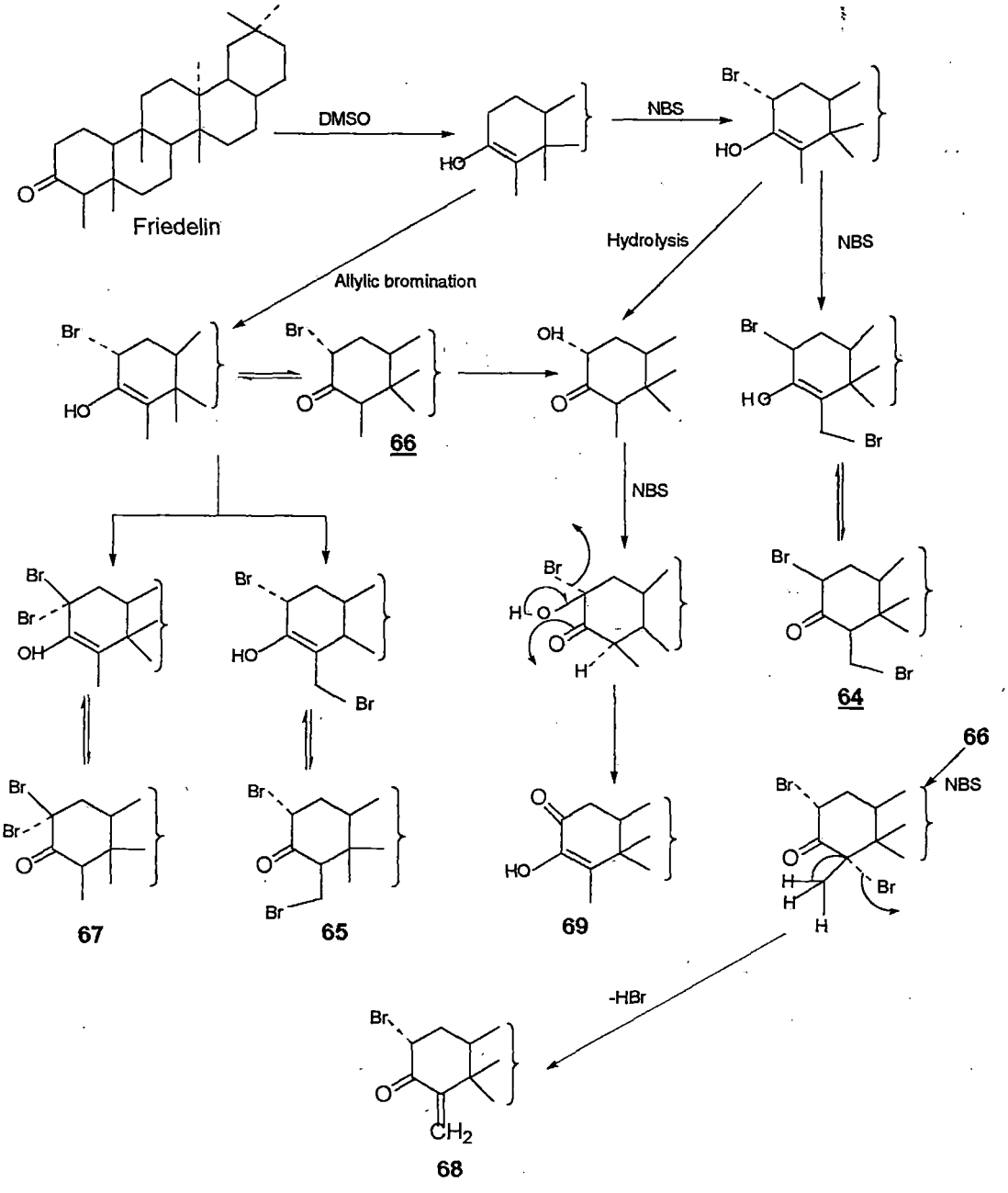
Compound **69** eluted by pet–benzene (3:2) was analyzed for $C_{30}H_{48}O_2$ and was analyzed as 2–keto–friedel-3(4)–en–3–ol.



69

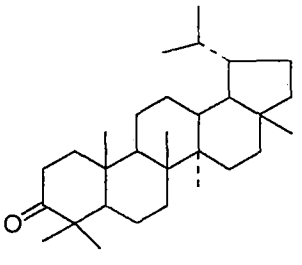
The mechanism proposed for the formation of six different products by the action of NBS in DMSO on friedelin is represented by **Scheme- V**.

Scheme V

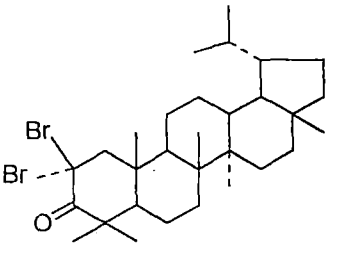


Pradhan *et al*[47] reported that lupanone **70** when treated with NBS in DMSO formed two different products **71** and **72** .

Compound **71** gave an intense green flame in Beilstein test indicating the presence of bromine. TNM test however was negative . Elemental analysis confirmed the molecular formula to be $C_{30}H_{48}OBr_2$ which was supported by the existence of three molecular ion peaks at M^+ 586, 584, 582 in the ratio of 1:2:1 proving the presence of two bromine atoms.The compound was assigned the structure 2,2 dibromo-lupan-3-one **71**.

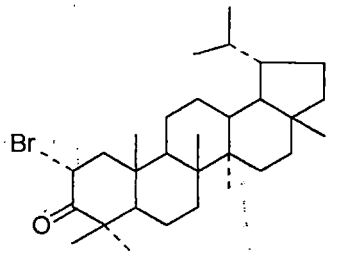


70



71

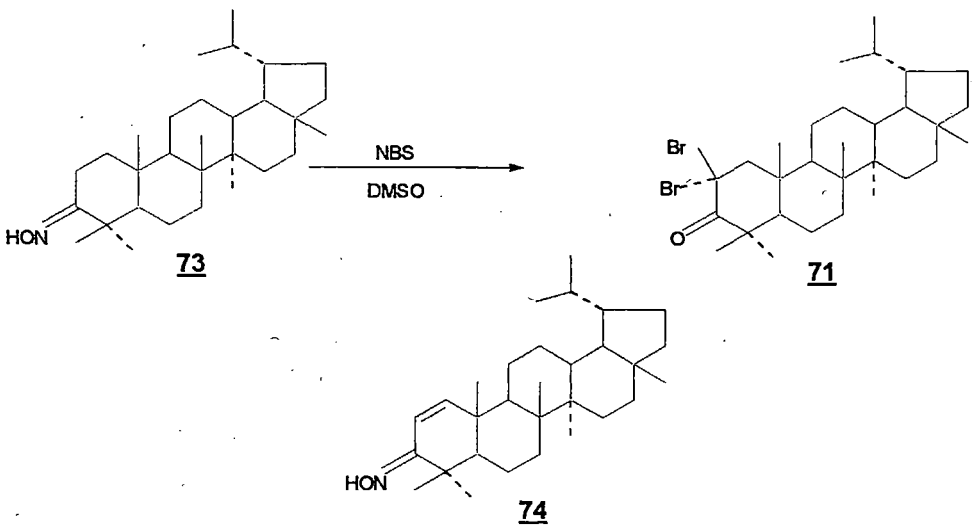
Compound **72** was analyzed for $C_{30}H_{49}OBr$ that showed a persistent green flame in Beilstein test. The compound was designated as 2α-bromo lupanone.



72

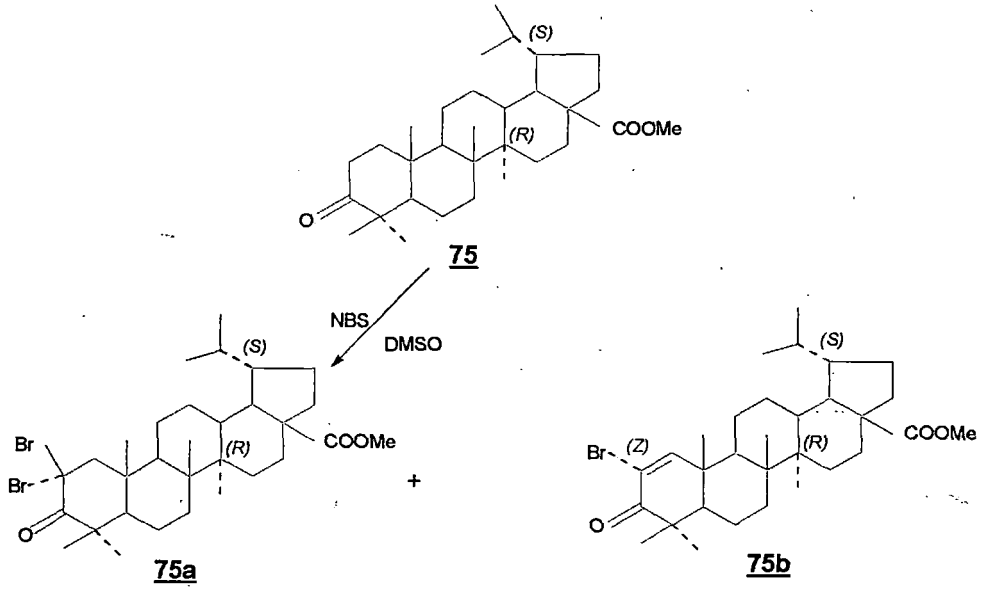
Pradhan *et al* [41] carried out the reaction of NBS on lupanone oxime **73** in DMSO and two products **71** and **74** were isolated by them. Compound **71** as indicated by elemental analysis had molecular formula $C_{30}H_{48}OBr_2$ and was assigned the structure 2,2- dibromo lupanone a compound identical with the one obtained from lupanone.

Compound **74** had the molecular formula $C_{30}H_{49}ON$ and was designated as lup-1(2)-en-3-oxime from analytical and spectral data.



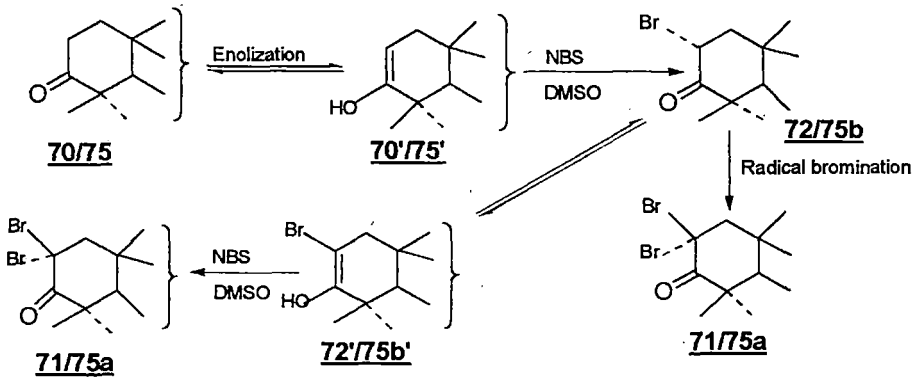
73 71 74

Similarly methyl dihydro betulonate **75** was treated with NBS in DMSO by Pradhan *et al* and two different products **75a** and **75b** were obtained .Compound **75a** had molecular formula of $C_{31}H_{48}O_3Br_2$ and was designated as 2,2-bromo methyl dihydro betulonate. Compound **75b** had molecular formula of $C_{31}H_{49}O_3Br$ and was assigned structure 2α-bromo methyl dihydro betulonate from spectral analysis.

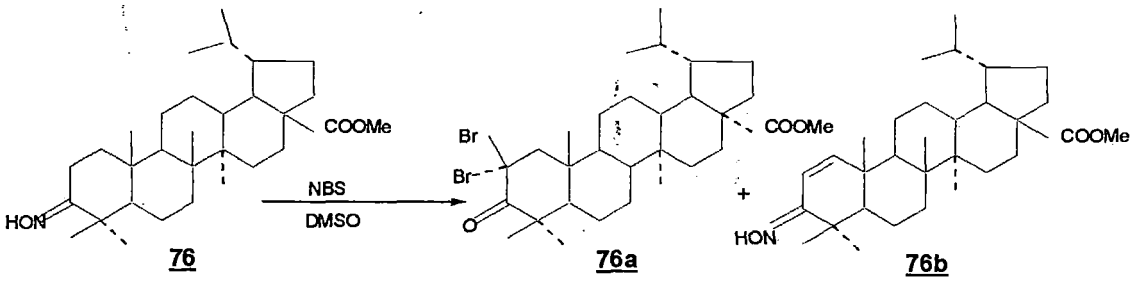


The mechanism for the acion of NBS/DMSO on lupanone and methyl dihydro betulonate was proposed as follows.

Scheme-VI

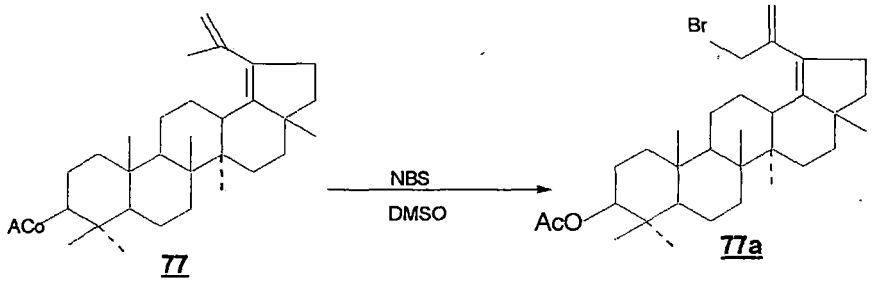


Two products **76a** and **76b** were reported by Pradhan *et al* by the action of NBS/DMSO on oxime derivatives of dihydro methyl betulonate **76.**



76 76a 76b

It was further reported by Pradhan *et al* [49] that 3β-acetyl lup-18(19), 20(29)-diene **77**_when acted on by NBS in DMSO furnished compound **77a** designated as 3β-acetoxy-30-bromo-lup-18(19), 20(29)-diene.



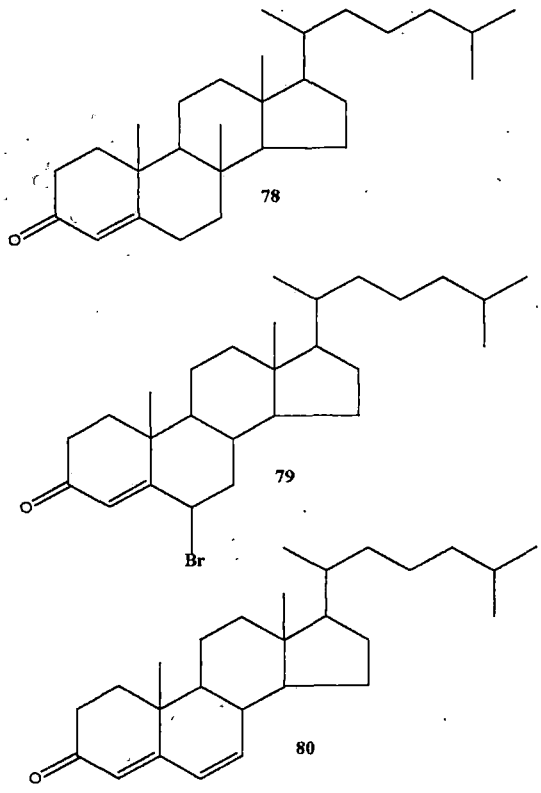
77 77a

CHAPTER-1 (SECTION-D)

BROMINATION & DEHYDROBROMINATION

N-bromosuccinimide as a reagent for allylic bromination has been used particularly for the introduction of supplementary double bond in cyclic system, the reaction is a two step process, bromination and dehydrobromination. A wide variety of base can be used in second step namely tertiary amine, pyridine, quinoline, γ-collidine etc.

$_{\Delta}$4- cholesten-3-one,**78** on allylic bromination by NBS gave 6-bromo compound **79** which on heating with collidine formed **80** , $_{\Delta}$4,6 cholestadiene-3-one.



N. Rubin *et al* [50] treated Δ 2(3)- acetoxy cholestene **81** with NBS. The enol acetate of cholestanone **82** (ring A/B trans) reacted with NBS in CCl_4 to give mixture of Δ^1 and Δ^4 cholesten-3-one **83** and **84** and 2-bromo cholestan-3-one **85.**